A STUDY ON BACTERIOLOGICAL PROFILE OF INFECTIVE ENDOCARDITIS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL

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BONAFIDE CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON BACTERIOLOGICAL PROFILE OF INFECTIVE ENDOCARDITIS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL"** is a bonafide record of work done by **DR.T.KANNAN ,** during the period of his Post Graduate study from 2016 to 2019 in the Institute of Microbiology, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai- 600003, in partial fulfillment of the requirement of **M.D MICROBIOLOGY** degree Examination of **The Tamil Nadu Dr. M.G.R Medical University to be held in May 2019.**

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DECLARATION

I, **Dr.T.KANNAN,** declare that the dissertation entitled **"A STUDY ON BACTERIOLOGICALPROFILEOF INFECTIVE ENDOCARDITIS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL"**submitted by me for the degree of M.D. is the record work carried out by me under the guidance of **Dr.J.Euphrasia Latha M.D.,** Professor, Institute of Microbiology, Madras Medical College, Chennai. This dissertation is submitted to The **Tamil Nadu Dr.M.G.R. Medical University, Chennai,** in partial fulfillment of the University regulations for the award of degree of M.D., Branch IV (Microbiology) examination to be held in May 2019.

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Introduction

INTRODUCTION

Infective Endocarditis (IE) is an infection of the endothelial surface of the heart or intravascular and prosthetic valves and intra cardiac device like pacemakers. IE can be classified according to location of vegetation and valve involved, the presence or absence of intra-cardiac devices and prosthetic valves and mode of acquisition (nosocomial, intravenous drug use related)[9]

IE is a continuously evolving disease with high morbidity and high mortality. In developed countries the incidence of IE is 1.7 to 6.2 per 100,000 persons per year. But in India, it seems to be around 14.5 per 100000 persons per year.[33&9] One of the major challenges in treating Infective Endocarditis is the changing demographics of the disease with respect to patient profile and microbiology. The evolution of IE diagnosis and management over the last 5 decades show continuous changes in clinical spectrum, etiological organisms profile and diagnostic methods, and significant geographic variations in the risk factors. In developed countries, more than 50% with IE episodes have normal heart valves, while rheumatic heart disease cause only 10 % case of IE [22]. But in India, RHD is still the most common predisposing condition.

Isolation of causative microorganism from blood culture is critical for diagnosis and planning treatment but in India the blood culture yielding positivity is only up to 40%.compared to western countries 80%.[22]

Increased incidence of IV drug abuse, improved and early detection of congenital heart disease, degenerative heart diseases, technological improvement in echocardiogram like Trans Esophageal Echo [TEE] ,increased incidence of health care associated infections in recent years might change the trend in clinical and microbiological profile. Many studies done in western countries uncovered and revealed the changed trend of IE in their regions, but such studies on IE in India particularly in South India is sparse.

Our study to know present epidemiological trend of IE ,the local prevalence of causative organisms and their antibiotic susceptibility in our locality to achieve improved outcome and reduce the mortality and morbidity caused by IE.

In this prospective study we analyzed the predisposing conditions, clinical profile and causative organisms and antibiotic susceptibility pattern and outcome of IE cases treated in a Tertiary Care Hospital, Chennai over a period of one year .

Aims &objectives

AIMS AND OBJECTIVES

- To study the bacteriological profile of Infective Endocarditis in a tertiary care hospital by conventional blood culture method

- Antimicrobial susceptibility testing will be done for all isolates on Mueller Hinton Agar by Kirby-Bauer Disc Diffusion method as per CLSI guidelines

Review of Literature

REVIEW OF LITERATURE

HISTORY:

The journey of IE starts from 16thcentury, William senhouse noted vegetations were found in cerebral, renal, splenic arteries of patients who had fever, heart murmur and purple spots.

Emmanuvel Wingse described the microorganisms in aortic valve in patients who had past skin suppurative lesions. Hugo Ribbert [1852- 1920] confirmed the relation of microorganisms with IE by injecting Staphylococcus aureus into rabbits and identified bacterial colonies on the surface of heart valves particularly in the mitral valve chordae tendineae.

Gulstonian lectures by William Bart Osler [1849- 1919] on malignant Endocarditis still stands as viable reference[1]. Lord Jeers Horder [1871-1955] an England physician published a collection of 150 cases of IE and he classified IE as acute, chronic, sub acute, fulminant and latent IE. Dawson and Hunter in 1945 used Pencillin to treat IE. Case defining page of IE is introduced by Charles Von Reyn et al in 1981[2]who distributed the IE cases as defined IE, probable IE, possible IE, and rejected IE by certain anatomical, pathological and clinical criteria.

The introduction of echocardiogram in cardiology changed the case defining criteria. In 1994 David Durack et al[3] at Duke university systematize the diagnostic criteria as definite IE, possible IE and rejected IE by major and minor criteria. In 2000 Jennifer. S.Li, a pediatrician at duke University completed the case defining Dukes criteria by certain modifications[4]

EPIDEMIOLOGY OF IE:

In last three decades noteworthy progress has been achieved in understanding of IE through various studies using different modifications in diagnostic criteria. The incidence of IE in developed countries is 1.7 to 6.2 per 100000 persons per year with 1 year mortality of 40%[9] but higher incidence reported in developing countries. The mean age of IE is above 50 years old in developed countries[44]. Nearly two third of cases occur in male gender but in India 76% of IE patients were younger than 50 years even though virtual fall of RHD as reported by ICMR study, done in school population in India [22].

Staphylococcus aureus surpassing Viridians Group Streptococcus as the etiological organism causing IE [khan et al] [21].due to IVD abuse and increased abuse of antibiotics and increased Prosthetic valve surgeries.

In Western countries 25 to 30%of Native valve Endocarditis were associated with health care activities like dialysis, prolonged IV catheters.

Congestive cardiac failure, renal impairment, prosthetic valve Endocarditis are independent predictors of mortality [14] but neurological complication, systemic embolism episodes and S.aureus infection also decide the outcome of IE management. The overall mortality in India is 24% to 41%.[14]

CASE DEFINITION:

The case definition of IE based on VonReyn's criteria till 1981 then Durack et al proposed new criteria for case definition by Duke's criteria based not only on blood culture but also on Echo findings to improve the and this improved the diagnostic yield sensitivity to 76%.[9] In 2000, Duke's criteria was modified to improve the specificity and sensitivity.

Inclusion of elevated CRP or ESR, presence of newly diagnosed clubbing, splenomegaly and microscopic hematuria as minor criteria has been suggested to improve the sensitivity by additional 10% but yet to get approval. [17]

The Modified Duke's Criteria for the Clinical Diagnosis of Infective Endocarditis [5 &26]

Major Criteria

1. Positive blood culture

Typical microorganism for infective endocarditis from two separate blood cultures.Viridians streptococci, Streptococcus gallolyticus, HACEK

group organisms, Staphylococcus aureus, or Community-acquired Enterocooci in the absence of a primary focus, **or**

Persistently positive blood culture, defined as recovery of a microorganism consistent with infective endocarditis from Blood cultures drawn >12 h apart; **or** All of 3 or a majority of ≥4 separate blood cultures, with first and lastdrawn at least 1 hr apart **or**

Single positive blood culture for Coxiella burnetii or phase I IgG antibody titre of >1:800

2. Evidence of endocardial involvement

Positive echocardiogram

Oscillating Intracardiac mass on valve or supporting structures or in the path of regurgitant jets or in implanted material, in the absence of an alternative anatomic explanation,orAbscess, orNew partial dehiscence of prosthetic valve, or New valvular regurgitation (increase or change in preexisting murmur not sufficient)

Minor Criteria

1. Predisposition: predisposing heart conditionsor injection drug use
2. Fever ≥38.0°C (≥100.4°F)
3. Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway lesions

4. Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots,rheumatoid factor
5. Microbiologic evidence: positive blood culture but not meeting major criterion,as noted previously, or serologic evidence of active infection with an organism consistent with infective endocarditis.

Definition of IE According to the Modified DukeCriteria[19]

Definite IE:

2 Major criteria, 1 major criterion and 3 minor criteria, or 5 minor criteria

Possible IE:

1 Major criterion and 1 minor criterion, or 3 minor criteria

Rejected:

1. Firm alternative diagnosis explaining evidence of IE
2. Resolution of IE syndrome with antibiotic therapy for ≤4 d
3. No pathological evidence of IE at surgery or autopsy
4. Does not meet criteria for possible IE as above

ETIOLOGY:

The causative organism for IE is mostly bacterial.[39] Staphylococcus spp, Streptococcus spp, Enterococcus spp, Listeria , Enterobacteriaceae, Pseudomonas spp, Acinetobacter spp, HACEK group bacteria, Brucella spp, and Chlamydia spp are causatives .

Candida ,Aspergillus and Histoplasmosis, Fastidious organisms like Bartonella spp, Legionella spp.,Coxiella burnetti, Tropheryma whipplei and Mycobacteria[39] and nutritional variant Streptococci[19] are reported as causative organisms rarely.

Although Staphylococcus spp. and Streptococcus spp. are collectively responsible for nearly 80% of IE cases the emergence of health care associated IE made an increase in the prevalence of Staphylococcal spp. against VGS which is showing declined prevalence in recent years.[44]

Staphylococcus aureus:

S.aureus is a part of normal human flora. The anterior nares is the common site of human colonization. S.aureus responsible for most of the acute and destructive IE .It is common cause of native valve Endocarditis and leading cause of prosthetic valve Endocarditis .S.aureus itself is an important cause of large vegetation which leads to embolic manifestations and right sided vegetation primarily in IVD abusers.

The emergence of methicillin resistant S.aureus pose serious consideration therapeutically.

The MRSA are identified rapidly by

- mecA detection by PCR
- mecA detection by oxoid latex agglutination test.
- Immunochromatographic strip assay for PBP2a.

MRSA are detected by disc diffusion test done using cefoxitin or oxacillin screen agar. Emerging resistance of MRSA strains even to vancomycin create an important awareness to detect susceptibility check with Daptomycin, Fosfomycin, Teicoplanin and Linezolid.

Staphylococcus other than S.aureus[CoNS]:

Over the past 30 years CoNS has been considered with little importance as important contaminant. But now due to increased invasive procedures ,it became an important agent of nosocomial infection. CoNS are accounting 7 to 11% of all native valve Endocarditis[30]. Of all the CoNS, S.epidermidis accounts 85% of native valve endocarditis and It is the most frequent cause of prosthetic valve Endocarditis. In prosthetic valves, the organisms infect the ring of sutures holding the valves, leads to the formation of microabscess. The organisms got entry while inoculated during surgery. S.hominis, S. lugdunensis, S.hemolyticus, S.capitis,,S.simulans, S.warneri, S.schleiferi, and S, xylosus are otherCoNS groups also cause Endocarditis. S.lugdunensis may cause unusual severe massive valve destructions. S.xylosus is associated with endocarditis due to IVD abuse.

Identification of Staphylococcus spp:[5] S.aureus is a gram positive cocci arranged in clusters and producing beta hemolytic colonies on blood agar, yellow pigmented colonies on nutrient agar.

Slide coagulase for detecting clumping factor is positive in S.aureus,S.lugdunensis and S.schleiferi sub schleiferi and negative in other Coagulase Negative staphylococcus .Tube coagulase is positive in S.aureus S .intermedius , S.delpheni, S.schleiferi sub coagulans and S.lutrea .[5]

Urea is hydrolysed in S.epidermidis and S.saphrophyticus, variable in S. aureus.Mannitol is fermented in S.aureus and not fermented in S.epidermidis and S.saphrophyticus. Staphylococcus aureus is producing phosphatase and DNAse while other staphylococci not producing . Ornithine decorboxylated in S. lugdunensis. Novobiocin sensitive organism is interpreted as S.aureus and S.epidermidis.while S.saphrophyticus is resistant.

Streptococcus species

Viridans Group of Streptococcus species cause subacute bacterial Endocarditis. Poor oral hygiene and periodontal disease, oral invasive surgery, upper GI endoscopy can cause transient bactermia that initiate vegetations on previously damaged cardiac valves.

VGS are known for multivalvular Endocarditis particularly bovis group. S.mitis, S.sanguinis, S.parasanguinis, S.oralis, S.gordonii, S.mutans, S.salivarius, S.vestibularis and S.sinensis are the VGS most frequently causing IE.

Neutropenia, Cytotoxic chemotherapy and Diabetes mellitus are important predisposers of VGS causing IE.

The streptococcus like organisms like Abiotrophia and Granulicatella are the causative organisms of 4-6% cases of IE[30& 45.] Originally they are called as nutritionally variant streptococci, require cysteine and pyridoxal for their growth in culture medias. Their importance stands here because of their resistant to many antimicrobial drugs. A.defectiva, G.adiacensare the commonest species reported. The Abiotrophia species were identified by its satellite growth along with S.aureus.

VGS - 5 major groups of species[30]

Mitis Group	S.mitis, S.oralis, S. Sanguinis, S. Para Sanguinis, S.gordonii, S.cristatus, S.peroris, S.infantis, S.australis, S.oligofermentis
Mutans Group	S.mutants, S.sobrinus
Salivarius Group	S.saliarius, S.vestibularis, S.infantarius, S.alactolyticus
Anginosus Group	S.anginosus, S.constellatus, S.intermedius
Bovis Group	S.bovis/S.equinus, S.gallolyticus subspecies, S.infantarius subspecies

The VGS are identified in Gram staining as Gram positive cocci arranged in pairs and chains, chains are elongated long chains. They produce alpha hemolysis mostly on blood agar.

The bile insolubility and nonfermenting inulin and resistant to optochin differentiate it from S.pneumoniae.

The bile esculin nonhydrolysis and no growth in 6.5% NaCL agar and no growth at 45 ^{0}C and PYR negative helps differentiate it from close Enterococcus group of organisms.[5]

Group	ADH	ESC	VP	ACID FROM MNTL	SOR
Mitis Group	V	V	-	-	-
Mutans Group	-	+	+	+	+
Salivarius Group	-	V	+	-	-
Anginosus Group	+	+	+	-	-
Bovis Group	-	+	+	V	-

+, positive reaction: - ,negative reaction:. v-variable :

ADH ,argininedihydrolase : ESC,esculin hydrolysis.:

VP ,Voges- Proskauer reaction .MNTL ,mannitol.: SOR,sorbitol.

The Bovis group is notable because adults with this VGS group isolation as bacteremia suggest the association of gastro intestinal neoplasms later.[34]

Enterococcus species

Enterococcus species are normal flora of GIT and less commonly biliary tract , vagina and male urethra. E.faecalis and E.fecium are accounting 90% and 5% of all enterococcal IE cases respectively.[27]

Nosocomial Endocarditis by Enterococcus emerge as significant hazard in this modern, surgical era particularly in patients age >50 years with degenerative heart disease, when undergo surgery for their GIT, GUT illness. Health-care-associated infection was also noted in an early retrospective review of 38 cases of Enterococcal IE published in 1970 By Mandell et al., in which 47% of infections had developed in elderly men who had undergone GU tract procedures or in younger women following gynecological procedures. Increased prevalence of instrumentation procedures of genito urinary tract and gastro intestinal tract procedures and surgeries all made Enterococcus as third leading cause of IE.[30]

The emergence of Vancomycinresisant Enterococci associated with serious life threatening infection. E.faecalis causing native as well as prosthetic valve IE. Enterococcus species are identified by Gram positive cocci arranged in pairs and looks like spectacle eyed appearance and producing mostly non hemolytic colonies on 5% sheep blood agar.

The specific characters, bile esculin hydrolysis, growth at pH 9.6 and growth at both 60 ^{0}c as well as 10^{0}Cand growth at 6.5% NaCL agar and PYR positive are helps to identify the organisms.[10& 40]

E.faecalis ferment pyruvate and sorbitol and hydrolyse hippurate and not ferment arabinose where as E.fecium ferment arabinose but not ferment pyruvate and sorbitol and also not hydrolyse hippurate.

Gram Negative Organisms

HACEK Endocarditis even though rare but associated with younger age group with immunological manifestation and associated with DM, PVE.[46] H.parainfluenza is the commonest cause of HACEK causing IE.

Regarding GNB causing IE ,approximately 40-60% of early onset PVE were caused by Gram negative organismsin one study done by KannePadmaja et al. [31]

Klebsiella pneumoniae and Pseudomonas spp ,Acinetobacter spp, Salmonella group D, Burkholderia cepacia and E.coli were also reported to cause IE in recent Indian studies by Padmaja et al, Abhilash et al and Senthilkumar et al .

Fungal Causes:

Though very rare the fungal etiology for IE is associated with immunosuppressed state and associated with large vegetation. Candida albicans, C.parapsilosis, C.tropicalis, C.glabrata and Histoplasmosis are important causative organisms.[21]

Anaerobes :

IE caused by Anaerobes are very uncommon.Finegoldia magna, Peptostreptococcus anaerobius, S.sacchrolyticus are Gram positive anaerobes causing IE[30] and Catonellamorbi, Sneathia sanguinegens are Gram negative anaerobic cause of IE apart from Bacteroides and Clostridiumspp.

Clinical Features of IE

The clinical spectrum of IE is highly variable depends on causative organism, preexisting cardiac lesions, presence of co-morbidities and other risk factors.

S.aureus, Streptococci and Pneumococci present as an acute course[.5] Subacute IE caused by Viridans Streptococci,Enterococcus, HACEK group organisms and CoNS.

The rare causatives like Coxiella burnetti,Brucella spp and Bartonella typically follows indolent course.

Fever is commonestsymptom[5]ofall of all IE . Pallor, Poorappetite, Weightloss, fatigue, Splinterhemorrhage, oslers Nodes, Janeway lesions, clubbing, splenomegaly, are common.

Skin petechiae, conjunctival haemorrhage, arthritis, arthralgia, Varying cardiac murmur ,bradycardia Congestive cardiac failure signs and symptoms like dyspnea, elevated JVP, hepatosplenomegaly and legedema and microscopichaematuira, Roth spots ,Haemiparesis, aphasia , seizure, splenic abscess or metastatic abscess due to embolisation,are clinical features of IE.

Lab manifestation:

Anemia,leukocytosis,microscopic haematuria,elevated ESR,CRP. Rheumatoid factor,decreased serum complement level are important laboratory manifestations .

IE caused by S.aureus, vegetation >10mm size ,mitral valve infection are associated with embolic-neurological manifestations and complications. Absence of fever is more common in elder age group, immune compromised individuals and IE caused by atypical organisms.

Risk Factors for IE :

- Previous H/o IE
- Previous cardiac disease
- Presence of prosthetic valve or Intracardiac devices like pacemaker
- H/o IVD abuse / presence of chronic I.V. access
- Presence of congenital heart disease
- Co-existing DM, HIV, Malignancy
- Contact with extensive health care system.[44]

Pre disposing heart disease :

Rheumatic heart disease is the commonest preexisting cardiac disease and was present in India.The studies in well developed countries shows around 40% cases of IE have preexisting degenerative cardiac disease.Congenital Heart disease accounts 28.6% of all IE cases in India . But it is only 12% in Western studies.[44] PVE are reported around 10-20 % of all IE [14] Mitral valves is affected in nearly half of in all IE in India.[N Garg et al &Abhilash et al]. VSD and Bicuspid aortic valve are reported as leading CHD cause for IE.[23]

Diagnosis of Infective Endocarditis:

Microbiological diagnosis:

Blood culture remains the cornerstone of IE diagnosis as well as in deciding antibiotics of choices.

Blood culture should be done before the commencement of antibiotics. Meticulous aseptic technique should be followed to reduce the risk of contamination with skin commensals[37].

Sampling should be obtained from peripheral vein not from indwelled vascular catheter.[34&37]

No evidence to support the theory, samples should be done from different sites[37]. But while taking sample from IVD abusers. The vein selected should not be the same vein they use for abuse.

Taking blood sample at different times is need to identify the bacteremia is constant which is the hall mark of Endocarditis. Blood culture positivity is more if the patient not received any antibiotics in the past 2 weeks.

In stable patients, the delay in initiation of antibiotics for 3 days increase the yield of culture diagnosis and discontinuation of antibiotics for at least 3 days helps to yield more positivity and improve the outcome and avoid improper, unnecessary antibiotics misuse.[17&34.]

Delaying blood sample with peaks of fever is having no rationale.[6] In unstable patients with IE, 2 sets of optimally collected blood culture samples at different times within 1 hour prior to commencement of empirical therapy is advisable to avoid undue delay in commencing treatment.[37&.9] Avoid wasting resources and time in getting anaerobic and fungal culture as a routine without strong clinical background to suggest the same.[17]

Contamination with skin flora during sample collection is common but that contamination rate should not be exceed 3%.[39]

The problem really arises when the isolate reported is CoNs which are indigenous microbial flora of skin. But could not be omitted as commensals because they are increasingly reported as cause of true bacteremia nowadays particularly in prosthetic valve.[30] . Isolation of 2 or

more isolates represent the same species from the same patient and further confirmation by molecular methods PCR solve this issue. [39*&19]

Sample Collection:

To reduce the chances of contamination, following steps to be followed while collecting blood sample by venipuncture .[30]

1. Wash with soap
2. Rinse with sterile water
3. Apply 1-2% tincture iodine or povidone-iodine
4. Allow to dry for 1-2 minutes for povidone iodine or 30 sec in case of tincture iodine.
5. Remove the iodine tincture with 70% alcohol wash.

- In General step 1 may be omitted. In case of povidone iodine use step 5 may be skipped. Tincture iodine, chlorhexidine glucoanate are superior to povidone iodine as per various studies.[39]
- After iodine –alcohol preparation, if need to palpate the site again, then the glove must be changed or disinfected.
- Syringe with needle is used to collect blood sample for culture .Blood culture bottles rubber septum can be disinfected with 70% alcohol swab .Changing the needles before injecting blood into culture media bottles is not recommended to avoid accidental needle stick injury.
- Blood culture media bottles to be stored at $4^{o}C$ when not in use.

- Before use (inoculation) bottles should be prewarmed to 25^{o}C.

Volume of Blood Samples:

Adequate sample volume of blood is necessary for better detection of bacteremia .The yield of results increased by 3.2% for every ml of blood collected. So the 10-20ml of blood per culture is required to increase the yield by 30%. [52]

For blood sampling from adults, 5-10ml of blood is collected and added to blood culture in 1:5 to 1:10 dilution .

For children 1-2ml of blood is collected and added to 20 ml volume blood culture bottles (1:10 to 1:20 dilution) .

Number of blood cultures samples:

- At least 3 sets of blood culture should be taken (1 aerobic and 1 anaerobic = 1 set) separated from one another by minimum 2 hours interval, over 24 hours.[5]
- Each culture bottle contains 50ml of medium [with 10ml of blood as added to that] is used.[6]
- If the initial 3 cultures are negative, 2 or more sets of culture can be obtained totally 5 sets overall.[19]
- Blood culture sampling should be done again if the patient is febrile even after 7-10 days of appropriate treatment[37]

Blood Culture Media:

The commercial blood culture bottles are multipurpose and nutritionally enriched.

- Trypticase soy broth&Brain heart infusion broth are the main culture media bottles recommended.
- Columbia CNA agar,Brucella Broth are also useful in appropriate places.
- Blood should be added directly in each lysis – centrifugation culture vials if the causative organism suspected is more likely to be Legionella, Bartonella and filamentous dimorphic fungus.[39]

Following Factors will improve blood culture yield:

- Take culture well before systemic antibiotic use (at least 3 days)
- More dilution of blood to broth (10-20ml blood per set) will improve results[17&39].
- Bacterial could not survive in clot, so adding anticoagulants like adding sodium polyanethalsulphonate 0.025% to 0.05% inactivate some antibiotics is broth particularly aminoglycosides in broth and acting as anticoagulant as well will improve the result .[45&30]
- Use of synthetic resin to culture bottles significantly improve the recovery of Enterococcus, S.pneumoniae and VGS.

Sample Transport:

Inoculated blood culture bottles should be transported to microbiological lab within 2 hours and incubate at 35^{o}C. [40] Refrigeration blood sample for culture is not recommended.Immediate transport of blood culture sample to lab for processing yield appropriate recovery and organism.

Sample Processing:

- Blind subculture is not routinely recommended in IE.
- Presumptive identification of positive blood culture based on Gram staining / acridine orange staining should be adapted to inform clinician to start presumptive antibiotics therapy.
- Blood culture broth should be incubated at 35-37^{o}C.
- Examine the evidence of growth during first 18 hours of collection by observing hemolysis, gas production of turbidity.
- Broth should be examined against bright fluorescent bulb or with incandescent transmitted light.
- Routine incubation for >7 days is not fruitful.[37 & 44]
- Subculturing should be done on blood agar, chocolate agar and MacConkey agar and finally on selective media if needed.

Extra care should be taken while opening broth bottles for subculture to avoid contamination. [40]

Some centres recommends 1 st sub culture on end of the day 1 itself 10 pm and then twice daily during first 2-3 days final subculture on 7^{th} day of collection [40] Extended culture incubation and subculture is advisable only in HACEK, Brucella like rare fastidious organisms

Routine Gram staining of macroscopically negative blood cultures (not turbid, no hemolysis) after 24 hours of incubation is not useful since 10^6-10^7 CFU are needed to produce turbidity while Gram stain detection upper level is 10^5 CFU only.[30] Acridine orange stains are better useful since their detection limit is $10^3 – 10^4$ CFU/ml.

Anaerobic culture:

Phenylethyl alcohol [PEA] anaerobic blood agar , Kanamycin – Vancomycin blood agar are useful for anaerobic sub culture.

Bact plus anaerobic / F, Bact / Alert (Standard anaerobic) are the blood culture broth available in commercially for anaerobic automated culture.

Recent studies suggest the processing for anaerobic culture should be limited to patients with abdominal disease process and clear cut strong evidence to expect anaerobes if exist.[30]Anaerobic culture may increase positivity by 6% only **if done selectively** .

Systems for processing blood culture Systems :

Manual Blood Culture Systems.

1.TheOxoid Signal Blood Culture System. [30]

Is a single-bottle blood culture system that detect the production of CO2 to identify early bacterial growth. After the blood sample collected , the sample has been inoculated into the main bottle, the signal chamber is connected by the needle inserted through the rubber stopper and positioned well below the surface of the culture medium. Growing bacteria produce CO2 resulting in increased pressure, which forces liquid into the signal chamber, this can be directly visualized and used to do subculture further .

2.BBLSepti-Chek Blood Culture System.

This system uses a standard blood culture bottle which contains either brain–heart infusion broth or trypticase soy broth. The bottle is designed for connection to a second plastic chamber that contains a paddle with agar surfaces. After the primary bottle was inoculated with the blood specimen, the plastic-contained “slide” is screwed on. This slide contains a trisurface paddle faced with MacConkey, and malt agar chocolate, , strips. The first “subculture” should be made after 4 to 6 hours of incubation at 35°C by inverting the bottle and thereby allowing broth to enter the slide’s chamber, thereby flooding the agar surfaces. Then the bottle should be again placed upright for continued incubation. The bottle should be inverted again at regular interval to reinoculate the agar media on the paddle.

Lysis-Centrifugation Blood Culture System

The Isolator system is widely accepted as an alternative blood culture method particularly useful for recovery of fastidious or slow-growing organisms like dimorphic fungi, Malassezia furfur and Legionella spp. Mean recovery time is reduced from 4.9 days using a conventional biphasic broth–agar system to 2.12 days for yeasts and 8.0 days for H. capsulatum compared with 24.14 days for the biphasic system.

The Isolator system considerd as the method of choice when quantitative cultures of blood was desired.

But increase in contamination rates over conventional systems is major problem with the use of the Isolator.

Automated and Computerized Blood Culture Systems.

1.TheBacT/ALERT Blood Culture System

Each capacity of blood culture bottle is to receive at least 10 mL of blood.If microorganisms grow in the blood–broth mixture, CO2 will be liberated , detected by a CO2-sensitive chemical sensor that is separated from the blood–broth mixture by a unidirectional CO2-permeable membrane is bonded to the bottom of each bottle.The color of the sensor turns from green to yellow in the presence of CO2. At every 10-minute intervals, a beam of light from emitting diodes (one for each well) is projected through an excitation filter to reflect off the CO2-sensitive sensor in the bottom of each bottle. The reflecting light will be directed through an

emission filter to a photosensitive detector which is connected to a computer compiler. As soon as the accumulation of CO2 is sufficient , an audible or visible “alert” is generated, and the sample position got positive is immediately flagged by the computer. Positive bottles can be immediately removed and further processed.

2.BACTEC Blood Culture Systems:

The BACTEC system consists of a self-contained incubator, agitatoranda detection device, similar to the BacT/ALERT 3D system.

The difference between theBacT/Alert and the BACTEC systems is that the latter uses fluorescent, not the spectral light to detect changes in the concentration of CO2 in the broth–blood mixture.

3.VersaTREKBlood Culture:

This system differs from the BacT/ALERT and the BACTEC systems in the following ways:

(1) the production of CO2 has been monitored manometrically,

(2) both gas consumption and production also monitored, and

(3) changes in the concentrations of H2 and O2 and CO2 are detected.

Reading occur during a phase of consumption of H2 and O2. Oxygen consumption will be accelerated at the time replicating organisms which enter the log phase of growth. A reading may be possible early in the incubation period even before a detectable amount of CO2 is produced .

Culture Negative IE:

CNIE defined as IE which by 3 or more sets of blood cultures are negative despite prolonged incubation. CNIE is important since it cause delay in diagnosis as well as delay in appropriate antibiotic selection.[42]

Negative blood cultures may be due to [51]

- Antecedent antibiotic therapy
- Presence of organism which does not grow on routine blood culture media.
- Suboptimal collection of sample
- Inadequate technique available currently to culture intracellular bacteria like Coxiella, Legionella and Bartonella
- Culture taken towards the end of a chronic course >3months of illness.
- Uremia
- Non infective Endocarditis.
- The overall blood culture negative IE is 35-60% in India. But it is only 10% in western countries.[17&33] In a study done at Chennai 2008-2010, the Negative culture accounts around 76%.

Further proceeding of CNIE:

- Extended incubation,
- Special media,
- Serological methods and

- Molecular diagnostic methods are useful to evaluate the culture negative cases further.

Extended incubation and subculture: [42]

- Subculture at 3 and 10 days.
- Prolonged incubation ≥21 days
- Using 20ml blood instead of 10ml

But all these measures should be done meticulously because intubation more than 7 days with regular interval subculture will leads to increased chance of contamination.[41]

Special medias:

1. 0.001% pyridoxal supplementation and 0.01% Cysteine to add with broth for Nutrional variant steptococci
2. Using middle brook and incubate for 6 weeks for Mycobacteria but not recommended as routine .
3. Brucella blood agar withhemin and vit k and incubation for Brucella.

Histopathological Staining of valve :

Surgical intervention for IE is performed in around 25% cases.

The excised valvular tissue should be processed for both microbiological and as well as histopathological / staining evaluation which are very useful in CNIE[19]

Brown – Hopps	-	Gram positive bacteria
Brown – Brenn	-	Gram negative bacteria
PAS	-	T.whipplei and fungus
Warthin starry	-	Bartonella spp.
Gimenez	-	Coxiella,Legionella
Macchiavello	-	Chlamydia

Excised cardiac valves may be processed for axenic culture on Columbia blood agar and chocolate agar supplemented with vitamin supplement at 35^{o}C for 15 days in 5% CO_2.[43 &51]

Serology:

Useful in diagnosing organisms like Coxiellaburnetti ,Legionella, Mycoplasma,andBartonella which are difficult to grow in culture.

- Single high titre or four fold rise from basal sample taken 2-4weeks apart are valuable.
- Single very high titre of IgG$\geq$800 is highly suggestive in case of Coxiella and Bartonella.[43]
- For Legionella single titre>256 is significant .

Molecular methods:

Genus specific / species specific with PCR ,Pan Bacterial / Pan fungal PCR are very useful in prior antibiotic started IE cases to identify the causative organisms.

PCR targeting the 16s RNA sequence to be performed.[51]18s, 28s RNA internal transcribed spacer are also used. Coxiella and Bartonela accounts37% and 20% of **identified pathogens** in CNIE ,while HACEK accounts 0.5% only and fungus etiology in 1% case.[42]

ECHOCARDIOGRAPHIC DIAGNOSIS OF IE:

Echocardiographic findings of Major Criteria are

1. Vegetation
2. Abscess or perivalvular involvement
3. New dehiscence of a prosthetic valve
4. Pseudoaneurysm and valve aneurysm
5. Perforation, fistula

The sensitivity of Trans Thoracic Echo in about 75%. But Trans Esophageal Echo in about 85% sensitive to detect vegetation.[50]

AHA recommends

- Trans Thoracic Echo should be done in all suspected IE
- TEE opted when TTE in negative and patient is having strong clinical suspicion.
- TEE / TTE should be be repeated if initial Echo suggestive of IE,to monitor development of fresh complication and to decide surgical intervention.

Complications of IE:

- Congestive cardiac failure
- Systemic embolization
- Periannular extension of infection
- Splenic abscess
- Mycotic aneurysm
- Intracranial mycotic aneurysm
- Neurological complication like CVA – ischemic / hemorrhagic stroke and cerebral abscess.

S.aureus, Streptococcus bovis group, , candida, Abiotrophia and HACEK and fungal Endocarditis are more associated with risk of embolization.[19]

Indication for Surgery

1. Persistent vegetation after systemic embolization
2. More than 1 Embolic events during first 2 wk of antimicrobial therapy
3. Increase in vegetation size despite appropriate antimicrobial therapy
4. Heart failure unresponsive to medical therapy
5. Valve perforation or rupture, Perivalvular extension Valvular dehiscence, rupture, or fistula Large abscess or extension of abscess despite appropriate antimicrobial therapy.

Special situations:

Prosthetic valve Endocarditis -PVE :

PVE accounts 10-30% of all IE

Early PVE - IE occurring within 1 year of surgery[5]

Late PVE - IE occur after 1 year of surgery

Early PVE is mostly nosocomial.Staphylococcus epidermidis, S.aureus, and HACEK account 65% all early PVE.

IE in IVDrug Abuse:

This estimated that 5-15% of IV drug abusers hospitalized for acute infection are having IE.[47]

Staphylococcus aureus, CoNS, streptococcus species,Pseudomonas species and Serratia marcescens are responsible for IE in IVDrug abusers . Mostly IVDrugabusers uses having vegetation in tricuspid value followed by aortic and then mitral valves.

S.aureus causes right sided IE where as Streptococcalspp .are causing left sided IE revealed by study by Maker et al.[48]

Anti -Microbial Therapy:

The prime goal of IE management is to eradicate infective organisms, sterilizing vegetations but high bacterial density, low metabolic activity of microorganisms and slow rate of growth, biofilm poses challenge in medical management.

The B-lactams and glycopeptidesare not much active against high bacterial density (10^8 - 10^{11} colony forming unit/ml) necessitates higher MIC than anticipated routinely (ie. 10^5 CFU/ml).[high inoculum effect][26&27]This high inoculum effect leads to emergence of antibiotic resistance.

The loss of pencillin binding proteins during stationary phase of growth leads to failure of Pencillin therapy in severe streptococcal infections. The bacterial effect of antibiotics can be enhanced by combination of antibiotics.Prolonged antibiotic therapy 2-6 weeks is necessary to sterilize the vegetations and eradicate organisms within vegetation. Increasing rates of MRSA and need of emergence of high MIC for vancomycin complicates the management.

Current evidence suggest that, For MSSA, flucloxacilinfor 6 weeks or cefazolinis recommended and for NVE[.5]

6 weeks Vancomycin IV plus 6weeks Rifampicin plus initial 2 weeks gentamycin is better choice in treating PVE caused by MRSA.

NVE - MRSA cases better managed with vancomycin alone . Daptomycin should be considered in Vancomycin resistant cases.

Streptococcal species:

The Pencillin resistance should be assessed in deciding the course and choice of antibiotics.

MIC <0.12 µg/ml strains are defined as Pencillin susceptible strains.

MIC >0.12 to 0.5 µg/ml are called as Pencillinrelativelyresistant strains

MIC more than 0.5 µg/ml are moderately resistant strain .

Pencillin susceptible strains should be treated with regime of 4 weeks Pencillin or Ceftriaxone alone for 4 weeks are the best choice of streptococcal management.[5]

In Pencillin relatively resistant strains,4 weeks high dose Pencillin plus 2 weeks gentamycin regime or vancomycin for 4 weeks may be used. [5]

In moderate resistant strains are better treated by 6 weeks high dose Pencillin + 6weeks Gentamycin Regimen or vancomycin 4 weeks .[5]

Enterococcus species:

6 weeks Ampicillin or high dose Pencillin with gentamycin is the regimen advised.[5]

In case of Pencillin allergy, vancomycin 6 weeks plus gentamycin in advisable. Enterococcus strains should be tested for susceptibility to Pencillin and vancomycin and also for high level resistance to gentamycin

to predict the synergistic interaction.Gentamycin resistant EnterococcusEndocarditis should be treated with Ampicillin plus Ceftriaxone.

HACEK and other organisms :

Ceftriaxone in reasonable for treating HACEKEndocarditis. Fluoroquinolones consider as alternative. Combination of Ceftriaxone or carbapenemsalong with gentamycin is considered as choice in treating Gram negative organisms.

Materials & Methods

MATERIALS AND METHODOLOGY

Place of study:

This cross sectional study was conducted in the Institute of Microbiology in association with Institute of Cardiology and Institute of Internal Medicine, Madras Medical College, Rajiv Gandhi Government General Hospital, Chennai-3.

Study period:

The study period was one year from April 2017 to March 2018 .

Ethical consideration:

Approval was obtained from the Institutional ethics committee before the commencement of the study. Informed consent was obtained from all the patients who participated in this study. All the patients satisfying the inclusion criteria were included. Patients were interviewed by structured questionnaire.

Statistical analysis:

Statistical analyses were carried out using Statistical Packages for Social Sciences (SPSS). The proportional data of this cross sectional study were using Pearson's Chi Square analysis test & Fisher Exact test.

Study Population:

3 sets of Blood culture samples were taken from Patients admitted with symptoms and signs suggestive of Infective Endocarditis in

RGGGH,Chennai and were transported to Microbiology Laboratory for bacteriological culture and antimicrobial sensitivity and important relevant data were collected during the collection visit.

Sample size: 60

Inclusion Criteria:

1. Age more than 18 years
2. Patient admitted with symptoms and signs suggestive of Infective Endocarditis and Echo cardiogram support the same as per modified Duke's criteria.

Exclusion Criteria:

1. Patients below 18 years
2. Patients not willing for blood sampling

Collection of Data:

During samples collection visit ,the following data were collected. Present Echocardiographic findings, Duration of fever, Previous history of any underlying Heart disease ,Previous heart surgery history ,history of IV drug abuse ,Recent Past Hospitalization before this illness, Short history of Present illness description ,other Laboratory investigation were noted.

After obtaining blood culture sample patient was followed up until he /she was inpatient in hospital and observed for the complication developed if later .

The case is defined as Infective Endocarditis by applying Modified Duke's criteria and they are classified as Definite IE and Possible IE.

Sample collection and processing:

Blood samples: 3 sets of blood culture samples were taken after informed consent, 2 hrs interval within 24 hrs in 3 different sites.

Meticulous aseptic technique followed.Personnel protective equipment precautions followed. The selected peripheral vein site is cleaned with sterile saline cotton swab. Then 1% tincture iodine is applied in and allowed to dry for 30 seconds. Then 70% alcohol is used to clean the area in same way.[30]

10 ml of blood was collected per culture bottle using disposable syringes and added to 40 ml of brain heart infusion broth in the sterile culture bottle.

Similarly 3 sets of blood culture samples were taken.

After collection of sample the needle and syringes were disposed as per Bio-Medical Waste Management Rules 2016.The collected samples were transported to Microbiology Lab immediately and incubated at 37° c for 48 hours. and observed for turbidity and visible haemolysis.

Then the samples were subculture on MacConkey agar, Blood agar and Chocolate agar for each set of sample irrespective of turbidity or other findings .and then incubated for 24 hrs

1. On MacConkey agar aerobically

2. On 5% sheep blood agar aerobically

3. On Chocolate agar in 5% CO2 and

On nutrient agar aerobically and observed for growth of isolates.Final subculture were done at the end of 7th day of collection. [40]

IDENTIFICATION OF CULTURE

The grown colonies morphology was noted with reference to their consistency, pigmentation, lactose fermentation, type of haemolysis.

Gram staining done from the observed isolates and identified as Gram positive or Gram negative organisms .

The Gram stain report was informed to the treating doctor as preliminary report.

The following biochemical test were done in Gram positive organisms: Catalase test, Coagulase test ,Bile esculin test, Vogues - Proskauer test, Urea hydrolysis, Sugar fermentation test[glucose,lactose, mannitol, sorbitol, arabinose, and pyruvate] Heat tolerance test, Arginine dihydrolysis test were done with appropriate controls.

Catalase test:

Tube catalase was tested by inoculating colonies in 3% Hydrogen Peroxide 0.5ml in a tube and observed for effervescence [40]

Slide coagulase test

was done by emulsifying the colony with 2 drop of saline in each of two circle drawn on glass slide and place a drop of rabbit plasma in one circle and mix with wooden applicator stick and rock the slide back and forth and observe for clumps .[30]

Tube coagulase:

was done by inoculating small amount of colony growth in 0.5 ml rabbit plasma in sterile tube- incubate for 4 hrs at 37° c and then at room temperature for next 18 hrs and observe for visible clot [30 &40]

Bile esculin hydrolysis test:

Done by inoculatecolony in bile esculin agar slant and incubate for 24 hrs at 35°c and observe for diffuse blackening of media was interpreted as positive.[30]

Voges- Proskauer reaction for Streptococcus species

was done by Coblenz method- adding alpha napthol 12 drops[VP reagent-A] and 4 drops of VP reagent –B[40% KOH +creatinine] to the 24 hrsincubated VP broth inoculated with colonies and observed for appearance of Red colour in 30 minutes which is indicative of Acetoin production for streptococcus species[10]

Urea hydrolysis test:

Urea hydrolysis was tested by inoculating loop full of colonies on to Christensen Urea medium slant and incubates at 35° c for 24 hrs and appearance of pink colour is taken as positive.

Sugar fermentation test:

Glucose, lactose,mannitol, sorbitol,arabinose,and pyruvate fermentation was tested by inoculating the colonies in 1% sugar medium tube and observed for production of acid and gas.

Phosphatase production test:

were tested by inoculating culture on phenolphthalein phosphate agar and incubate at 35°c for 24hrs and the pour 4 drops of ammonium solution after inverting the plate lid and the phosphatase producing organism turn bright pink in few minutes. [10]

DNase production test:

was done by Spot inoculation of colonies on to DNase medium and and incubate for 24 hrs at 37° c and observe for growth. [10]

Growth at45°c **[Heat tolerance test]:**

Was done by inoculating the colonies in peptone water and kept in water bath at 45°c for 30 minutes[40page 269,271] and then inoculating on nutrient agar and incubate at 37 ° c for 24 hrs and observed for growth[40]

Growth in 6.5% NaCL:

was tested by inoculating the colonies in 6.5% NaCL broth and incubated at 37°c for 24-72 hrs and observed for growth[40]

Moeller's decorboxylation test:

[Ornithine decorboxylation /Arginine Dihydrolysis] was tested by inoculating the culture colonies into a tube with Ornithine decorboxylase media /Arginine Dihydrolysis media and sterile mineral oil is overlaid and incubated at 35°c for 1-7 days along with base control and observed for the initial yellow colour formation which then change to deep purple colour due to alkalinisation by ammonia production while control base is remain yellow. [40.]

Sensitivity to Novobiocin:

was tested by Novobiocindisks [30µg] impregnated on MHA with lawn culture of inoculum and incubate at 37 °c for 24 hrs and observe for zone of inhibition16 mm or more. [30]

Optochin sensitivity test:

was done by impregnating 5 µg optochin disks [6mm disk] over the lawn culture of organisms in sheep blood agar plate, and incubating at 37° c for 24 hrs . The zone of sensitivity 14 mm or more is favour of Streptococcus pneumoniae whileViridans Group Streptococci are resistant to optochin. [40 &10.]

In Gram negative organisms,

Catalase, Oxidase, Hugh-Leifson OF glucose test, Nitrate reduction test ,Indole, Methyl red ,Voges-Proskauer reaction ,Citrate utilization test ,Urea hydrolysis were done with appropriate controls.

Oxidase test:

Done by wet filter paper method by using 1% tetra methyl paraphenylenediaminedihydrochloride and appearance of deep purple colour within 10 seconds was taken as positive .

Hugh -Leifson OF glucose test :

was done by inoculating the colonies using straight wire, stabbing the OF glucose medium three to four times half way to the bottom in each of two tube and one tube is covered with 1 cm layer of sterile mineral oil leaving the other tube and incubating at 35° c for daily and observing fermentative pattern –acid production in both tubes or oxidative pattern – acid production in open tube or asaccharolytic pattern – no acid production in both tubes

Indole production:

was tested by , inoculating tryptophan broth with test organism and incubate at 37° c for 24 hrs and add Kovac's reagent through inner side of test tube and observe for appearance of bright fuchsia red colour at the interface of the reagent and the broth which is interpreted as positive. [30]

Triple sugar iron agar [TSI] :

was tested inoculating test organism on to TSI medium by stabbing through the centre of medium to the bottom and then streaking on slant and incubate for 18 - 24 hrs at 37 ° c for sugar fermentation and acid production –yellow colour and production of gas and H2S production.[10]

Citrate Utilization :

Is tested by inoculating a well isolated colony from primary isolation medium onto Simmons citrate medium slant surface and incubate for 24 hrs at 35° c and development of deep blue colour indicate as the test organism is utilizing citrate.

Methyl Red test for mixed acid production

Inoculate the MR broth with a pure culture of the test organism and incubate the broth at 35°C for 24- 48 hours. And then add 5 drops of the Methyl red reagent directly to the broth, the development of a stable red colour in the surface of the medium is interpreted as positive.[30]

VP (Voges-Proskauer) Test (Barritt's Method) for Gram-Negative Rods

Add 0.6 ml (6 drops) of solution A (alpha-naphthol) and 0.2 ml (2 drops) of solution B (KOH) to 1 ml of VP broth and shake well after addition of each reagent. and observe for 5 minutes. Red colour, interpreted as positive and Yellowcolour as negative. [10]

Motility of organism was tested by Hanging drop method .

The following organisms were identified and processed further by the specific tests.

Staphylococcus aureus was identified as below:

Morphology &Biochemical test	**Results**
Colony morphology	Beta haemolysis on 5% sheep blood agar Yellow pigmented colonies in Nutrient agar
Gram stain	Gram positive cocci arranged in clusters
Tube Catalase	Positive
Coagulase test	Slide and tube coagulase positive
Urea hydrolysis test	Urea hydrolysed
Phosphatase test	Producing phosphatase
Sugar fermentation	S.aureus- Ferment mannitol.
Novobiocindisk sensitivity	Sensitive

Enterococcus species were identified as below:

Morphology and Biochemical tests	**Result**
Colony Morphology	Magenta collared colonies in MacConkey agar Tiny non haemolytic colonies in Blood agar
Gram stain	Gram positive cocci arranged in ovoid pairs and chain
Tube catalase	Negative

Bile esculin test	Positive
Growth at 45°c	Growth present
Growth at 6.5%NaCL	Growth present
Sugar fermentation test	E.faecalis -Ferment mannitol,pyruvate and sorbitol producing acid but not ferment arabinose E.fecium- Ferment mannitol and arabinose producing acid but not pyruvate and sorbitol
Arginine dihydrolysis	Dihydrolyse arginine and producing ammonia.[40]

Viridians Group Streptococci Mitisgroup was identified as below:

Morphology and biochemical test	**Result**
Colony morphology	Alpha haemolytic colonies in Blood agar and no visible growth in MacConkey agar
Gram stain	Gram positive cocci arranged in long chains
Tube catalase	Negative
Voges-proskauer reaction	Negative
Sugar fermentation test	mannitol and sorbitol not fermented.
Arginine dihydrolysis	not producing ammonia from arginine [30&40]
Optochin sensitivity	Resistant

Klebsiella pneumoniae was identified as below:

Morphology and Biochemical test	**Result**
Colony morphology	Mucoid lactose fermenting colonies on MacConkey agar
Gram stain	Short plumby Gram negative bacilli
Motility	Non motile organism
Tube catalase	Positive
Oxidase	Negative
Huge –Leifson OF test	Fermentative pattern
Indole test	Negative
TSI agar	Producing A/A acid in butt /acid in slant with gas production
Citrate utilization test	Utilize citrate
Urea hydrolysis test	Hydrolysis urea
MR test	Negative
VP test	Positive

Pseudomonas aeruginosa was identified by

Morphology and biochemical test	Result
Colony morphology	Non lactose fermenting colonies in MacConkey agar and diffuse bluish green pigmentation in Nutrient agar
Gram stain	Gram negative bacilli
Motility	Motile
Tube catalase	Positive
Oxidase test	Positive
Hugh –Leifson OF test	Oxidative pattern
Indole	Negative
Citrate utilization test	Utilize citrate
TSI agar	Alkaline butt / alkaline slant with no gas and no H2S
Urea hydrolysis test	Negative
Arginine dihydrolysis	Produce ammonia from arginine

Antimicrobial susceptibility test:

Antimicrobial susceptibility testing for the isolates was done using Kirby-Bauer disc diffusion method on Mueller- Hinton agar [MHA].

The CLSI guidelines were used to interpret the zone of diameter.

Medium used:

MHA for S.aureus, Enterocooci and Gram negative organisms

MHA with 5% sheep blood agar for Viridans Group Streptococcus .

Inoculum: 0.5 McFarland standardized colony suspension from sheep blood agar.

Incubation : at 37° c for 18-24 hrs incubation

Preparation of inoculum:

Around 4-5 individual colonies of similar morphology were picked up with bacteriological straight wire and inoculated in peptone water and incubated for 4 hrs and matched with 0.5 McFarland standard.

A sterile cotton swab is dipped into that peptone water then excess broth is removed by pressing against the tube wall then swabbed in three directions to ensure equal complete distribution of inoculums over the entire MHA plate. Maximum 6 disc were used in a single plate .The distance between each disc should be minimum at least 24 mm from centre to centreof the disks. Zone of diameter was interpreted according to CLSI guidelines for respective organism.

The following standard strains were used for confirmation of quality of disks.

1. Staphylocoocusaureus –ATCC 25923
2. E. coli-ATCC25922
3. Pseudomonas aeruginosa –ATCC 27823
4. The following panel of drugs disks were included in antimicrobial susceptibility testing for the relevant organisms as below

Staphylococcus aureus :

Antimicrobial agent	**Disk content**	**Sensitive [mm]**	**Intermediate [mm]**	**Resistance [mm]**
Pencillin [**Pen]**	10 units	≥29	-	≤28
Erythromycin [**Ery]**	15µg	≥23	14-22	≤13
Clindamycin [**Clin]**	2 µg	≥21	15-20	≤14
Ciprofloxacin[**Cip]**	5 µg	≥21	16-20	≤15
Tetracycline [**Tet]**	30 µg	≥19	15-18	≤14
Trimethoprim–sulfamethaxazole **[CoT]**	1.25/23.75 µg	≥16	11-15	≤10
Chloromphenicol [**CK]**	30 µg	≥18	13-17	≤12
Rifampin[**Rif]**	5 µg	≥20	17-19	≤16
Linezolid [**Lz]**	30 µg	≥21	-	≤20
Cefoxitin	30 µg	≥22	-	≤21

- Vancomycin susceptibility was tested by MIC breakpoints by Epsilometry method and Vancomycin screen agar
- Cefoxitin was used to for detection of Methicillin Resistance.

Enterococcus species :

Antimicrobial agent	Disk content	Sensitive [mm]	Intermediate [mm]	Resistance [mm]
Ampicillin[**Amp]**	10µg	≥17	-	≤16
Erythromycin	15µg	≥23	14-22	≤13
Chloromphenicol	30 µg	≥18	13-17	≤12
Rifampin	5 µg	≥20	17-19	≤16
Linezolid	30 µg	≥23	21-22	≤20
Vancomycin	30 µg	≥17	15-16	≤14

- **High level gentamycin** susceptibility also tested for Enterococcus species

Viridans Group Streptococci:

Antimicrobial agent	Disk content	Sensitive [mm]	Intermediate [mm]	Resistance [mm]
Ceftriaxone [**CTR]**	30 µg	≥27	25-26	≤24
Erythromycin	15µg	≥21	16-20	≤15
Clindamycin	2 µg	≥19	16-18	≤15
Ofloxacin[**OF]**	5 µg	≥16	13-15	≤12
Tetracycline	30 µg	≥23	19-22	≤18
Chloromphenicol	30 µg	≥21	18-20	≤17
Linezolid	30 µg	≥21	-	-
Vancomycin	30 µg	≥17	-	-

- Pencillin susceptibility was tested by MIC breakpoints.

Klebsiella pneumoniae :

Antimicrobial agent	Disk content	Sensitive [mm]	Intermediate [mm]	Resistance [mm]
Ceftriaxone	30µg	≥ 23	20-22	≤19
Piperacillin-tazobactam **[PT]**	100/10 µg	≥ 21	18-20	≤17
Meropenem[**Mer]**	10 µg	≥ 23	20-22	≤19
Amikacin[**AK]**	30 µg	≥ 17	15-16	≤14
Gentamycin	10 µg	≥ 15	13-14	≤12
Ciprofloxacin	5 µg	≥ 21	16-20	≤15
Trimethoprim – sulfa methaxazole	1.25/23.75 µg	≥ 16	11-15	≤10
Tetracycline	30 µg	≥ 15	12-14	≤11
Chloromphenicol	30 µg	≥ 18	13-17	≤12

Pseudomonas aeruginosa:

Antimicrobial agent	Disk content	Sensitive [mm]	Intermediate [mm]	Resistance [mm]
Ceftazidime[**CTZ]**	30µg	≥ 18	15-17	≤14
Piperacillin-tazobactam	100/10 µg	≥ 21	15-20	≤14
Meropenem	10 µg	≥ 19	16-18	≤15
Amikacin	30 µg	≥ 17	15-16	≤14
Gentamycin	10 µg	≥ 15	13-14	≤12
Ciprofloxacin	5 µg	≥ 21	16-20	≤15

Detection of Resistance mechanism:

IA. To detect Methicillin Resistance in Staphylococcus aureus by using Disc diffusion method :[clsi]

Inoculum: 0.5 McFarland turbidity standardized inoculum of S.aureus from blood agar is used.

Disk : Cefoxitin 30 µg disk.

Medium : Mueller –Hinton agar

QC Recommended : S.aureus ATCC 25923

Test procedure:

The inoculums is swabbed on to the surface of MHAgar in three dimension and Cefoxitin disk is placed and incubated for16-18 hrs at33°c-35°c.

Interpretation:

Result is interpreted as if the zone size≤ 21 mm = *mecA*positive and ≥ 22 mm = *mecA*negative.

Cefoxitin is used as a surrogate for mec-A mediated oxacillin resistance. Isolates that test as mecA positive should be reported as oxacillin[methicillin] resistant strains.

1. B. Vancomycin Agar Screening for Staphylococcus aureus and Enterococcus spp by agar dilution method: [vancomycin MIC≥8µg]

Preparation of antibiotic stock solution

Vancomycin stock solution was prepared by using

Formula: W =1000 xV x C/P

Where, V= Volume of the stock solution to be prepared [10 ml]

W = Weight of antibiotic in mg to be dissolved in volume V in ml

P= Potency of the antibiotic in relation to base

C = Final concentration of solution,

Antimicrobial concentration: 6µg of vancomycin

Inoculum: colony suspension standardized to0.5Mc Farland.

Medium: BHI agar

Recommended QC: E .faecalis ATCC 29212

Procedure:

Using a micropipette, spot a 10µl of suspension onto agar surface.

Incubation : at 35°c for 24 hrs.

Observation : examine in transmitted light for > 1 colony growth.

Interpretation : >1 colony = reduced susceptibility to vancomycin [clsi]

1C. Epsilometry test for Vancomycin resistance:

It is a double ended MIC graded paper E strip [EZY MIC ™ STRIP] contain vancomycin and teicoplanin on a single strip in a concentration gradient manner .The upper half is coated vancomycin concentration graded tapering downwards and capable of showing MIC range of 0.5 to 32 µg/ml where as the lower half is coated with teicoplanin drug concentration in reverse direction to show MIC in range of 0.5 to 32 µg/ml.

Inoculum : from overnight growth on BAP, standardized to 0.5 Mc Farland

Medium : BHI agar plate

Procedure:

The inoculum is swabbed on BHI agar plate in three directions and then the double ended E strip was kept on agar and incubated at35°c for 24 hrs. Interpretation: Read the MIC value where the edge of inhibition ellipse intersect the side of strip

Organism	**E strip MIC interpretive criteria µg /ml [clsi]**		
	Sensitive	**Intermediate**	**Resistance**
Staphylococcus aureus	≤2	4-8	≥16
Enterococcus faecalis	≤ 4	8-16	≥32

1D. Detection of Inducible Clindamycin Resistance in Staphylococcus spp:

Method : Disk diffusion [D - zone test]

Medium : MH Agar

Antimicrobial concentration:

15µg of Erythromycin and 2 µg of Clindamycin disks spaced 15- 26mm apart.

Inoculum : colony suspension standardized to 0.5 McFarland

Incubation : at 35°c for 16-18 hrs

Observation& Interpretation:

1. Flattening of the zone of inhibition adjacent to erythromycin disk [D zone] =Inducible Clindamycin resistance
2. Growth within the zone of inhibition around Clindamycin = Inducible Clindamycin resistance even if no D –zone.

1E.Detection of High Level Amino glycoside Resistance in Enterococcus spp [clsi]:

Method : Disk diffusion

Antimicrobial concentration: 120µg gentamycin disk

Medium : MHA

Inoculum : colony suspension standardized to 0.5 McFarland

Recommended QC: E.faecalis ATCC 29212

Incubation: at 35°c for 16-18 hrs

Interpretation: if the zone of inhibition ≥10 mm =susceptible

7- 9mm = inconclusive

6mm = resistant

1 F. Detection of Pencillin MIC break points in Viridans Group Streptococci by Epsilometry method:

Inoculum : from overnight growth , standardized to 0.5 McFarland

Medium : Mueller –Hinton agar supplemented with 5% sterile ,defibrinated blood

Procedure:

The inoculum was swabbed on Mueller –Hinton agar supplemented with 5% sterile, defibrinated blood agar plate in three directions and thenPencillinEzy MIC ™ Strip [0.002-32µg/ml] was kept on agar plate and incubated at35°c for 24-48 hrs in 5% carbon dioxide.

Read the MIC value where the edge of inhibition ellipse intersects the side of strip.

Interpretation: [clsi]

Organism	PencillinMIC break points[µg/ml]		
	Sensitive	Intermediate	Resistance
Viridans Group Streptococci	≤0.12	0.25 -2	≥4

Results

RESULTS

Table 1.Classification of Infective Endocarditis based on modified Dukes criteria in 60 cases.

Type of IE	Native valve Endocarditis	Prosthetic valve Endocarditis	Intra cardiac Device associated Endocarditis	Total [n=60]
DEFINITE IE	28	9	0	**37**
POSSIBLE IE	18	4	1	**23**
Total	46	13	1	**60**

Definite IE cases : 62%[37 cases]

Possible IE cases : 38% [23 cases]

Native valve Endocarditis : 77% [46 cases]

Prosthetic valve Endocarditis : 21.3% [13 cases]

Intra cardiac device associated Endocarditis : 1.7%[1 case]

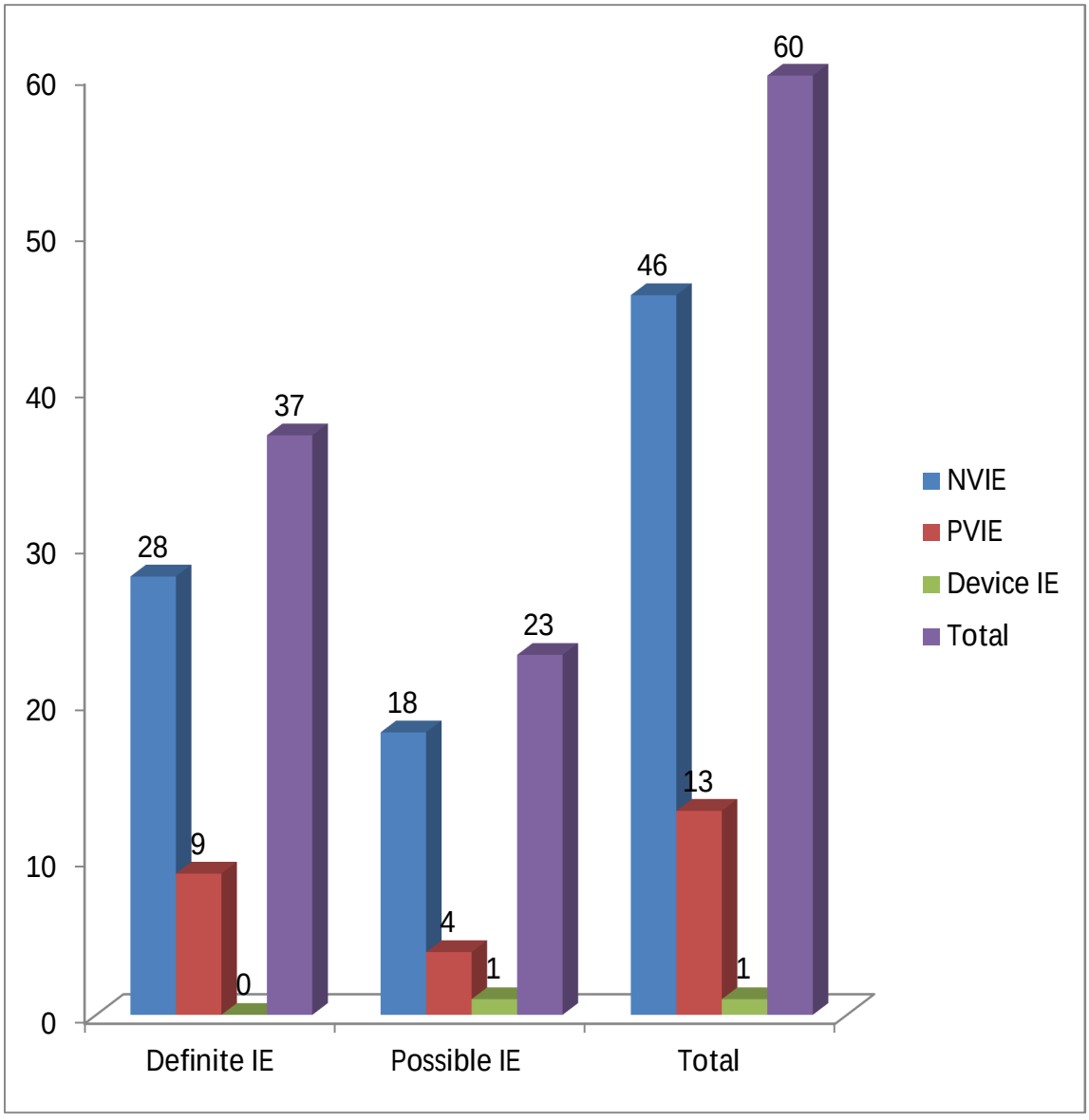


Fig.1.Classification of IE on the basis of modified Dukes criteria in 60 cases

Table 2. Age and sex wise distribution of 60 patients

Age	Male	Female	Total[n=60]	Percentage
18-30	10	13	23	38%
31-40	8	8	16	26%
41-50	10	3	13	22.7%
51-60	2	0	2	3.3%
>60	3	3	6	10%
Total	**33**	**27**	**60**	**100%**

Around 64%of patients are belongs to age less than 40 years .

Only 13.3% patients belong to age more than 50 years.

The mean age of this study population is 37.25±14.23.

Minimum age is 19years and maximum age is 75 years.

Male female ratio is 1.2:1

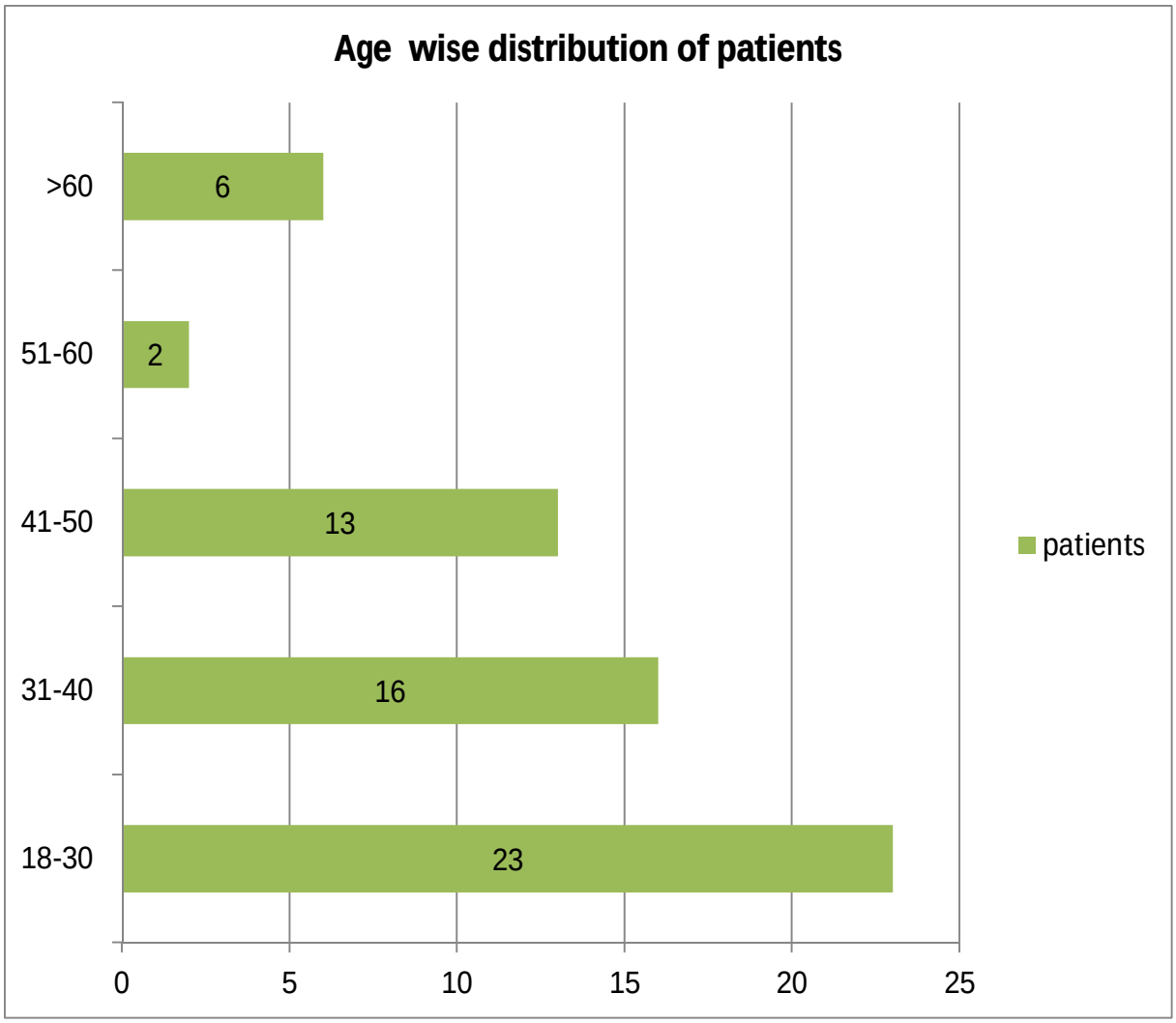


Fig.2 Age wise distribution of patients

Table 3. Clinical profile of 60 cases

Presenting symptoms	No. of patients [n=60]	Percentage %
Fever	59	98%
Dyspnea	24	40%
Arthralgia	13	21.6%
Chest pain	23	38.3%
Wt.loss	7	11.6%
Loss of appetite	6	10%

Presenting signs	No. Of patients [n=60]	Percentage %
Splenomegaly	28	46%
Clubbing	23	38.3%
Pedal edema	13	21.6%
JVP raised	11	18.3%
Petechiae skin lesion	14	23.3%
Anemia	13	21.6%
Infarct & Embolic manifestation	9	15%
Jaundice	2	3.3%

Regarding clinical symptoms fever is the most common presenting feature followed by dyspnea and chest pain.

Splenomegaly and clubbing were the most common presenting signs.

Around 21 % of patients presented with leg edema at the time of admission.

Around 21% of patients admitted with anemia**.**

Around 21% patients are admitted with Health care associated IE category since they were on regular dialysis / recent admission for other illness in past 60 days.

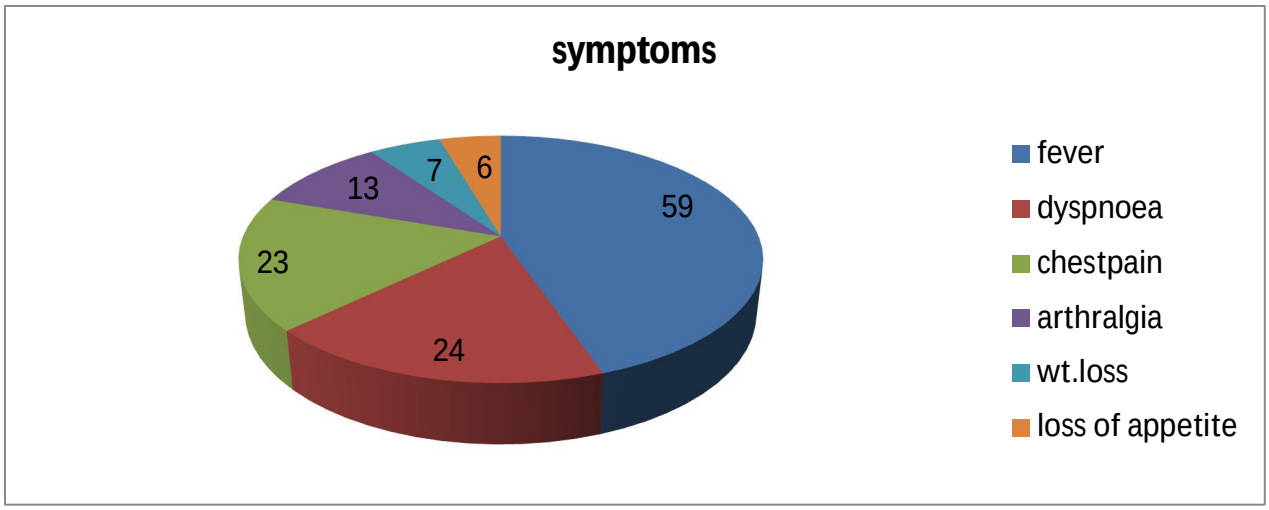


Fig .3 Clinical symptoms frequency of 60 cases

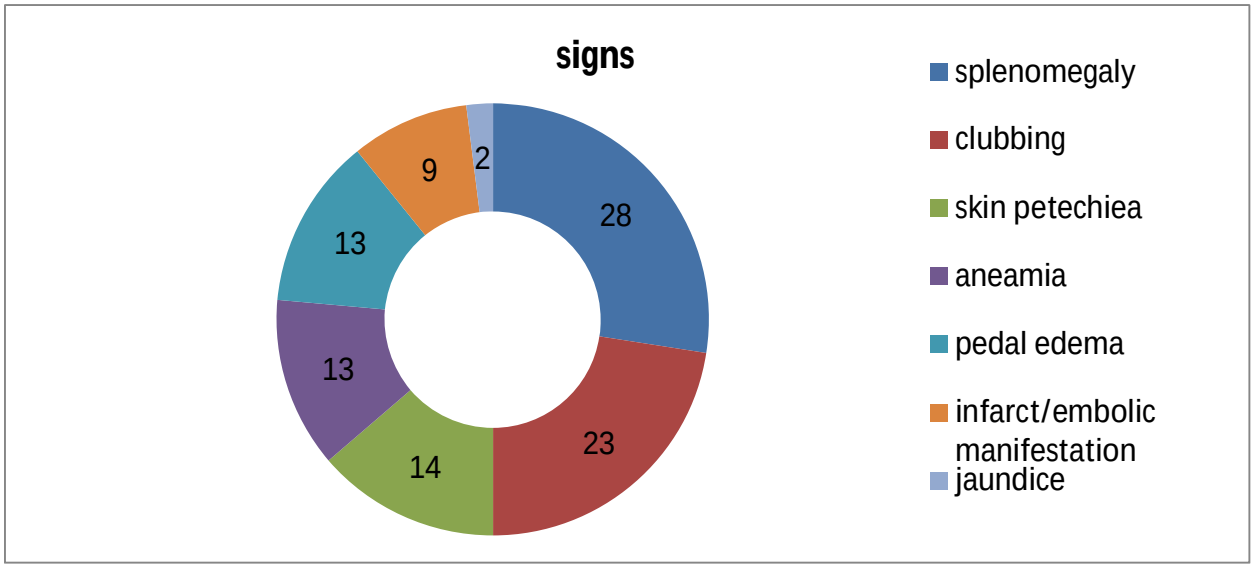


Fig 4. Clinical Signs of all 60 cases

Table 4. Predisposing conditions and underlying heart disease in all 60 cases

Previous Underlying heart disease already known.	No. Of patients [n=60]	Percentage %
Rheumatic heart disease	**36**	**60%**
Mitral valve disease	29 [48.35%]	
Aortic valve heart disease	7 [11.65%]	
Congenital heart disease	**9**	**15%**
Bicuspid aortic valve	3 [5%]	
VSD	6 [10 %]	
Other cardiac conditions [including Heart block ,coronary artery disease]	**4**	**6.6%**
No previous underlying heart disease diagnosed already before the current episode of IE	**11**	**18.4%**
Total	**60**	**100%**

Rheumatic heart disease is the most common predisposing underlying heart disease at the time of admission 60%.

Mitral valve disease contribute 48.3%andaortic valve disease in 11.6%

Congenital heart disease is predisposes in 15% of cases, of which VSD contribute 10% and Bicuspid Aortic valve account 5%

Around 18.4% of patients admitted with not a known heart disease at the time of admission, later they were determined to have RHD

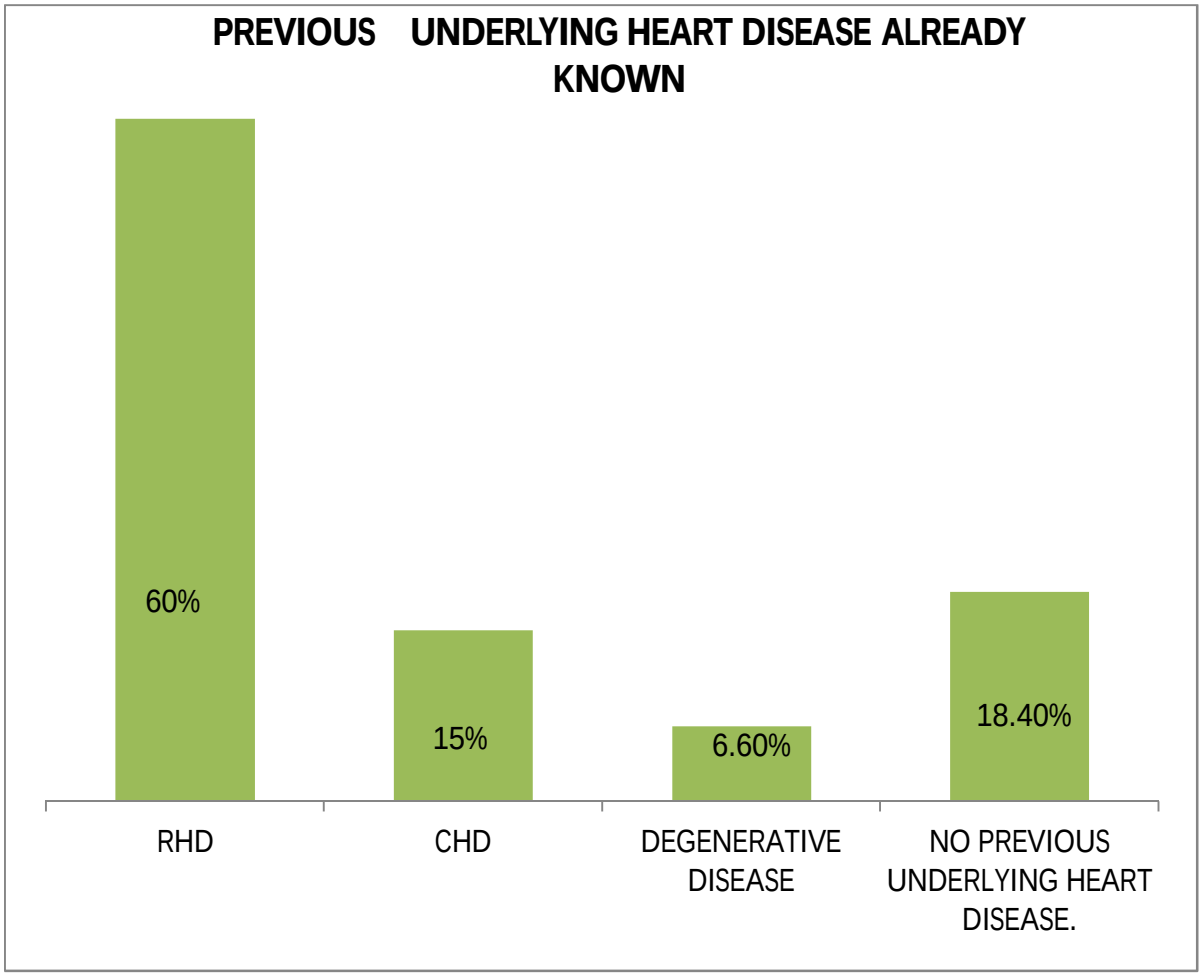


Fig 5. Previous underlying heart disease already known

Table 5. Co- Morbid condition associated with admitted patients

Co morbid condition	No. of patients [n=60]	Percentage %
Diabetes	6	10%
Systemic Hypertension	12	20%
Chronic Renal failure	6	10%
Chronic liver disease – HbsAg positive	1	1.7%
Seizure	4	6.7%
Hypothyroidism	2	3.3%
Residual hemi paresis with recent stroke	3	5%
Admitted now withHemiparesis [stroke]	6	10%
Alcoholic	1	1.7%
Heart block	1	1.7%

21.7 % of patients admitted with neurological co- morbidity [seizure and stroke]

10 % of patients had diabetes mellitus.

Alcoholic habitat is found only in 1.7%

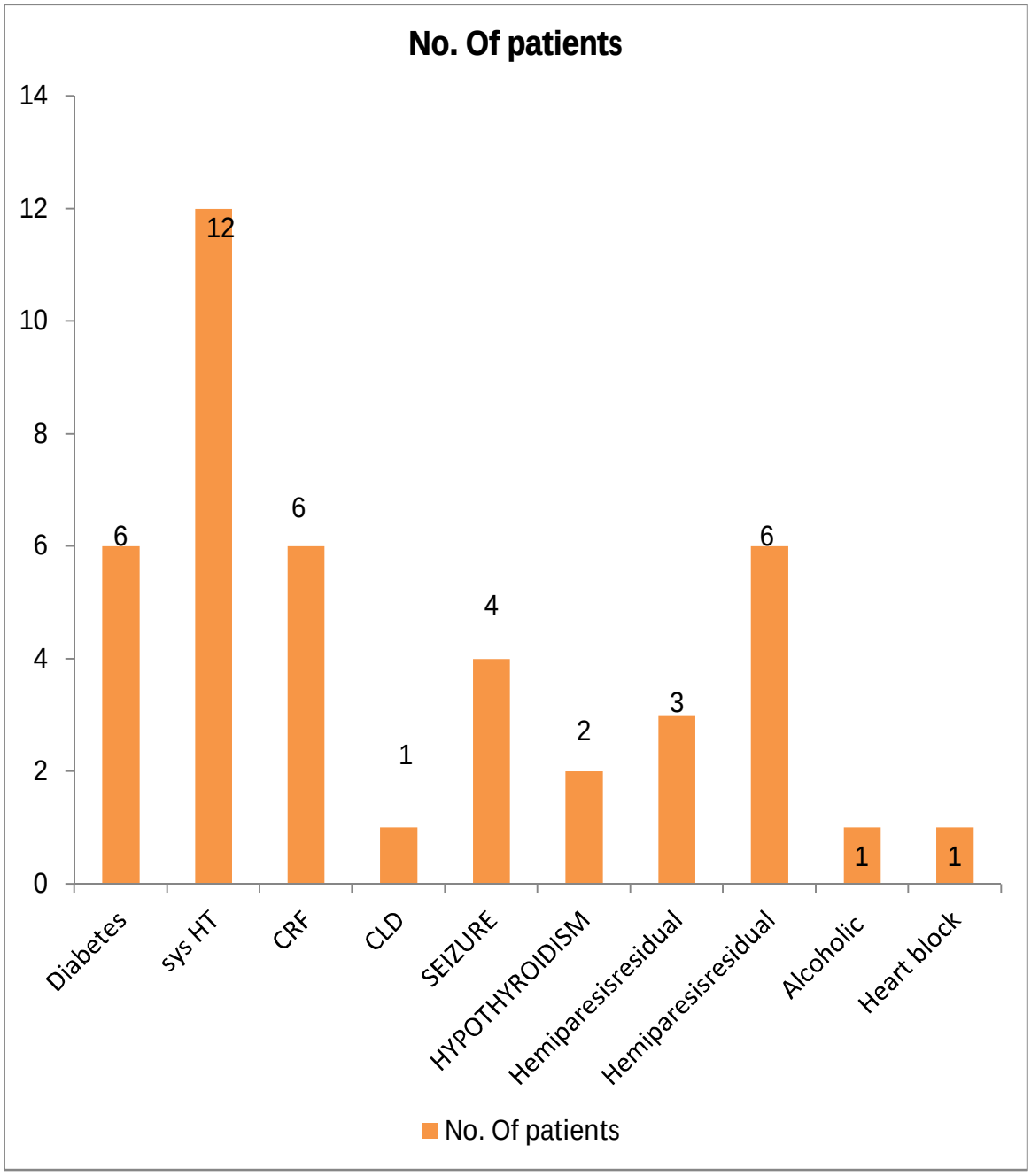


Fig 6.Co-morbid conditions in 60 cases

Table 6. Echocardiographic [Trans Thoracic Echo] findings

Echocardiographic finding	No. Of patients [n=60]	Percentage
Vegetation in AML	15	25%
Vegetation in PML	12	20%
Vegetation in RCC	4	6.6%
Vegetation in LCC	5	8.4%
Vegetation in NCC	2	3.3%
Vegetation in Ring of Prosthetic valve[both mitral/aortic]*	6	10%
Paravalvular leak/dehiscence	3	5%
Chordae tendineae rupture /Torn leaflet	2	3.3%
Paravalvular Abscess	1	1.7%
Vegetation in other site[Tricuspid/device]	3	5%
No vegetation or related findings	**7**	**11.7%**
Total	**60**	**100%**

* Including Additional 2 cases - vegetation - is detected by Trans Esophageal Echocardiography.

Table 7.Valves affected in this IE episode in 60 patients

Valves involved	No. of Patients [n=60]	Percentage%
Mitral	34	56.7%
Aortic	16	26.5%
Tricuspid	2	3.4%
Pulmonary	0	0
Intracardiac device	1	1.7%
Others[Echo negative for vegetation}]	7	11.7 %
Total	**60**	**100%**

Mitral valve 56% is the predominantly affected valve .

Aortic valve is involved in 27% of patients

Tricuspid valve is involved in 3.4 %cases.

Echo is negative for vegetation in 11.7 % of patients

Around 10 cases [17 %] were found to be in size more than 10 mm.

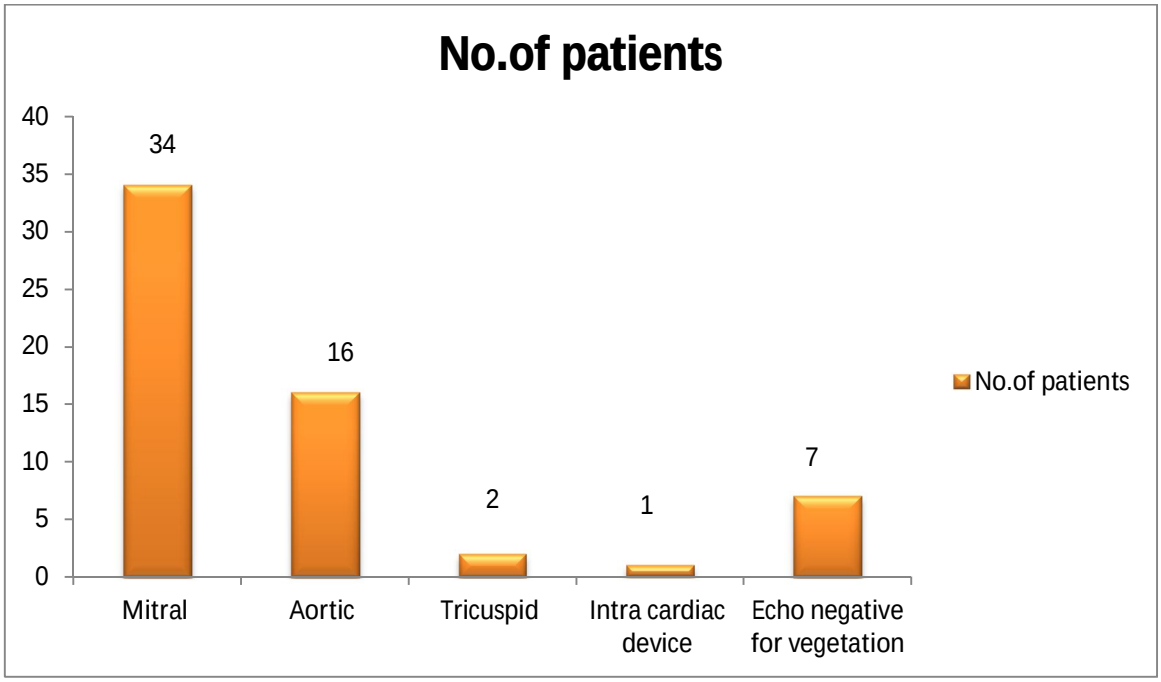


Fig.7. Valves affected in 60 cases

Table 8.Echocardiographic Detection of Vegetation in PVE and NVE

Valve type	Echo positive [for Vegetation or related findings]	Percentage %
Native valve[46]	42	91%
Prosthetic valve[13]	10	77%
Device[1]	1	100%

P value 0.015 –significant

Around 91.3% of NVE cases and 77% of PVE cases shows positive Echocardiographic findings [Major criteria.]

Table 9.Blood Culture Results

Culture result	3 positive	2 positive	1 positive	Total [n=60]	Percentage %
Culture positive	2	9	6	**17**	**28.3%**
Culture negative	0	0	0	**43**	**71.7%**

Out of 60 patients in our study, 17 cases were reported as Culture Positive [28.3%].Of the positive culture patients 2 patients show all three culture positive and 9 patients reported two culture positive.6 patients found to have single culture positive.

Table 10. Blood Culture positivity in different categories of IE

Type of IE	CPIE[n=17]	CNIE[n=43]
Native valve IE [including definite and possible IE]	14 **[82%]**	32 **[74.7%]**
Prosthetic valve IE [including definite and possible IE]	3 **[18%]**	10 **[23%]**
Device associated IE [including definite andpossible IE]	0	1 **[2.3%]**
Total	**17 [100%]**	**43 [100%]**

Around 82 % of Culture Positivewere found to be NVE.

Only 18% of culture positive were found to be PVE .

The culture was Negative in the only one case of Device Associated IE in our study.

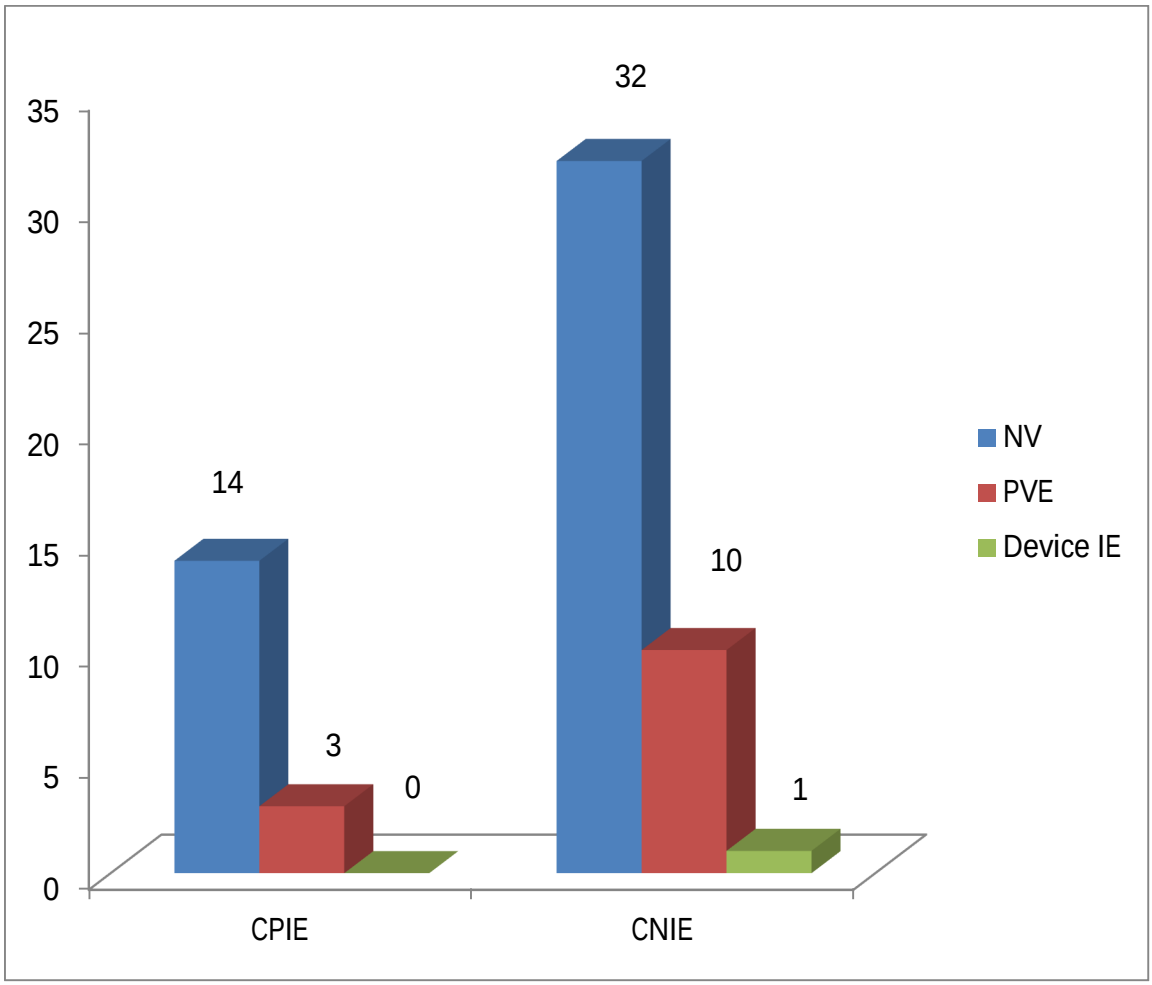


Fig 8.Blood Culture positivity in different categories of IE

Table 11. Complications developed during the course of illness

Complications	Total No of patients n=60
Congestive cardiac failure	**23** **[38%]**
Stroke	**9** **[15%]**
Renal impairment[acute on chronic]	**6** **[10%]**
Septic shock	**2** **[3.4%]**

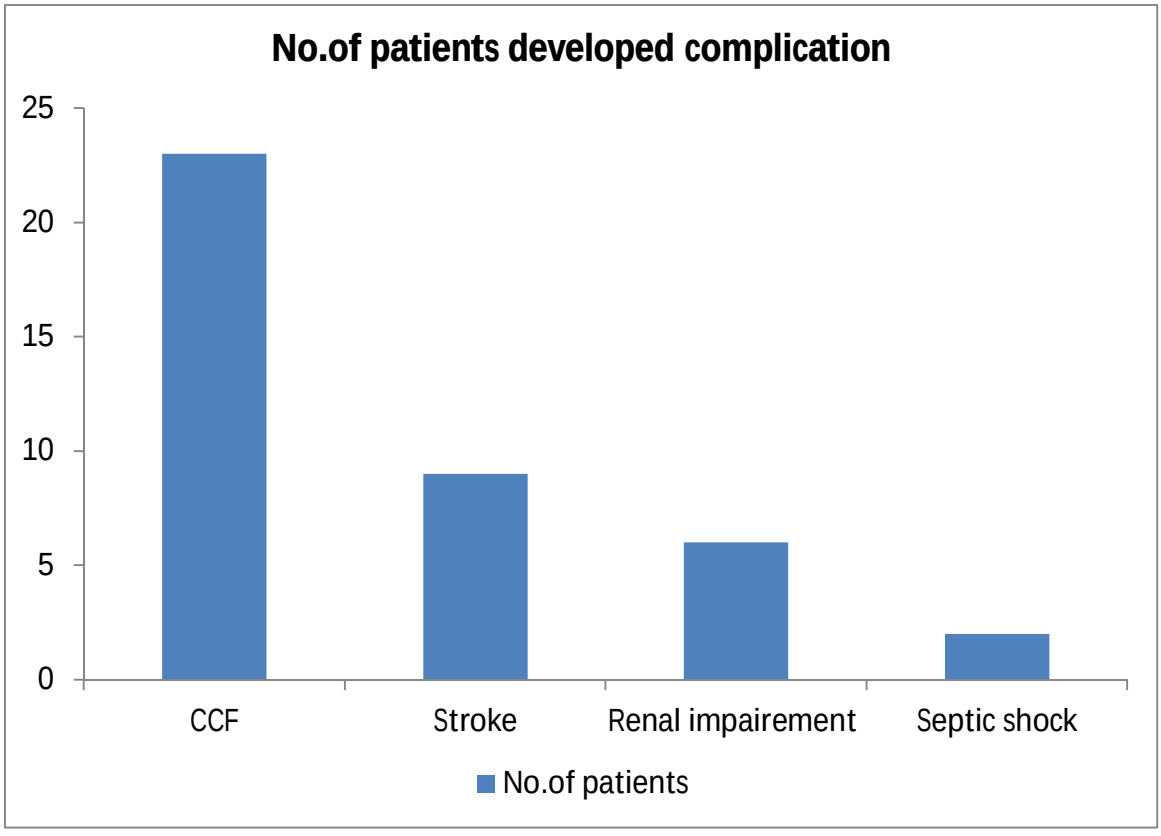


Fig 9. Complications developed in 60 cases

23 patients admitted in our study were developed Congestive Cardiac Failure during the course of illness.[38%].

[Of the 23 cases of CCF , 5 cases were also developed worsening of renal impairment also and 2 cases also with septic shock]

Total of 9 patients were the Stroke complicating Infective Endocarditis.

[3 patients had recent stroke with residual Hemi paresis].

Septic shock developed in 2 patients. .

Worsening of renal parameters happened in 6 cases

Table 12.Complication pattern in CPIE vs CNIE cases

Complications	Culture positive IE	**Percentage [n=17]**	Culture negative IE	**Percentage [n =43]**
Congestive cardiac failure	11	**64.7%**	12	**27.9%**
Stroke [residual+now]	5	**29.4%**	4	**9.3%**
Renal impairment [acute on chronic]	2	**11.7%**	4	**9.3%**
Septic shock	2	**11.7%**	0	**0%**

Of the 17 Culture Positive patients

64.7% patients developed CCF. **[P value <0.05**]

29.4 %patients reported to have Stroke complicating IE

11.7% patients had worsening of Renal parameters and

11.7% patients developed Septic shock.

In 43 cases of CNIE

CCFdeveloped only 27.9**%** cases.

Stroke was reported in around **9.3 %** cases.

Renal parameters worsening happened only in around **9.3 %**cases

Septic shock developed in none of CNIE cases

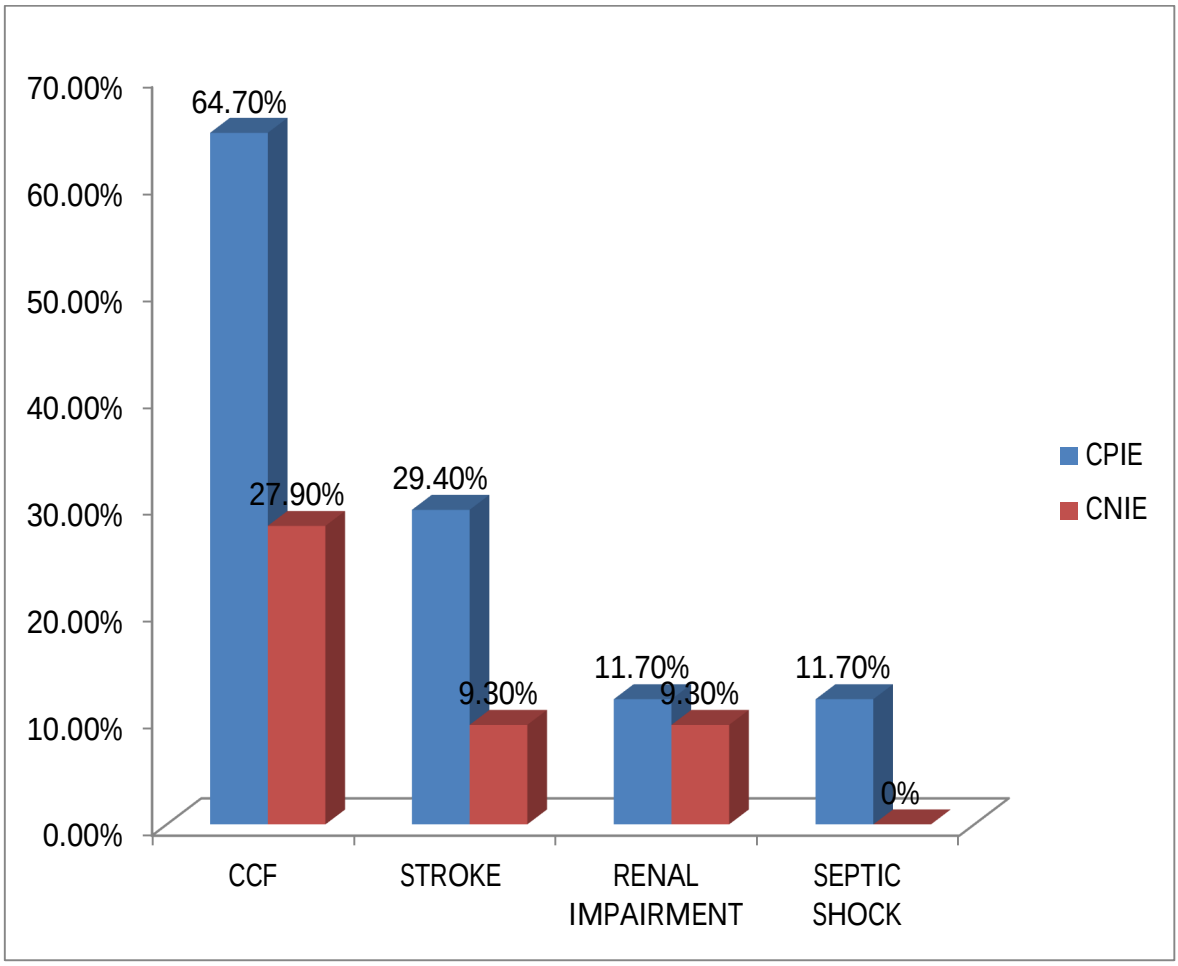


Fig.10. The comparison of complication developed in CPIE and CNIE cases

Table 13. Management

MANAGEMENT	Recovered	Not recovered	Lost follow up	Total no. Of Patients n=60
Medical Management	37 [67.3%]	6 [10.9%]	12 [21.8%]	55 [91.7%]
Surgical management	0	5 [100%]	0	5 [8.3%]

P Value < 0.05-significant

- 5 cases were treated by surgical line of management [prosthetic valve dehiscence /leak- 2 cases. Peri annular abscess 1 case , chordae structure rupture – 1 case . Refractory CCF -1 case] .
- Other 55 cases were treated by medical line of management.
- All the 5 cases of surgically managed cases were not recoverd
- 6 cases of Medically managed were not recovered during the hospital stay.
- The patients who went against the medical advice due to poor prognosis were also determined as not recovered.Totally 12 patients were lost their follow up.

Table 14. In hospital Mortality analysis

Cause of death	No .of patients [11]	**Percentage [n=11]**
Congestive cardiac failure	6	**55%**
Stroke [residual+now]	2	**18%**
Renal impairment[acute on chronic]	1	**9%**
Septic shock	2	**18%**

- Totally 11 patients were not recovered from this illness
- Refractory CCF was reasoned for 6 cases of 11 not recovered [55% of mortality]
- 2 patients were not recovered due to septic shock ---18% of mortality
- 2 Stroke complicating IE patients were went against medical advice due to poor prognosis.
- 1 patient went against medical advice due to worsening of renal failure [along with CCF]

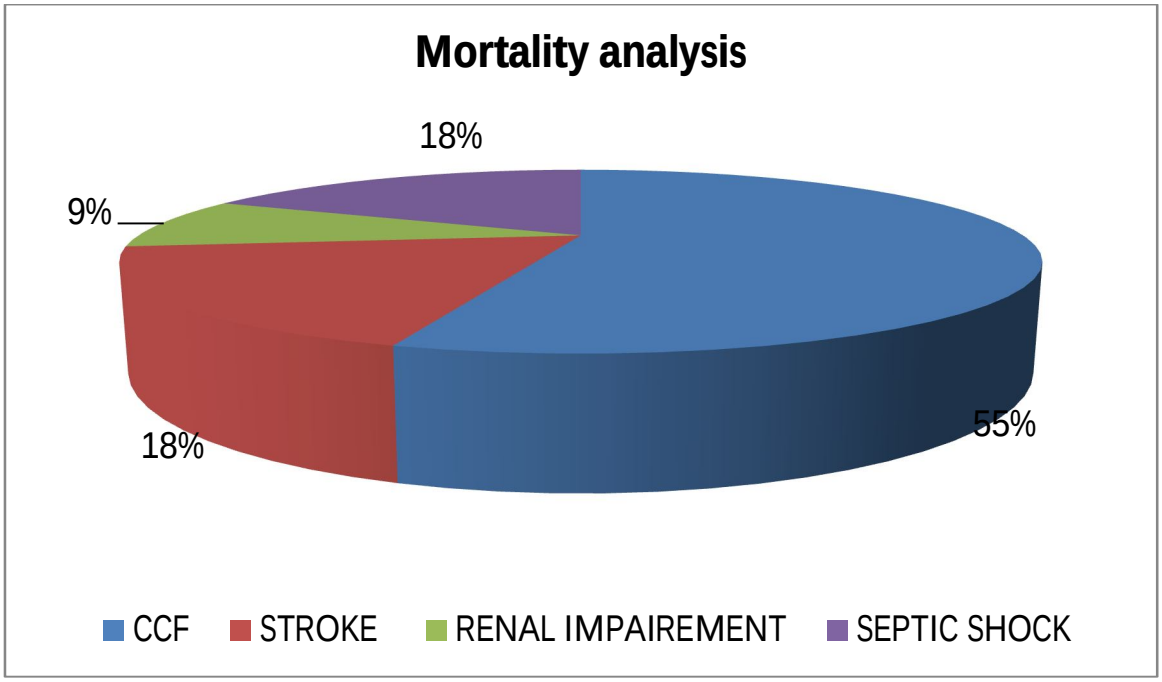


Fig 11. Mortality analysis

Table 15.A Comparison of NVE and PVE

Characters	**NVE [n=47]**		**PVE [n=13]**	
Echo positivity	42	**91%**	10	77%
Culture positivity	14	**31%**	3	23%
CCF	19	41%	3	23%
Stroke	6	13%	3	23%
Renal impairment-	6	13%	0	0%
Septic shock	2	5%	0	0%
Surgical line of management	3	6.5%	2	15%
In hospital mortality	**7**	**15%**	**4**	**30%**

Table 16. Organisms isolated in Blood culture samples

Organisms	No. of Isolates]	Percentage
Staphylococcus aureus MRSA	5	8.2%
Staphylococcus aureus MSSA	2	3.4%
Enterococcus faecalis	4	6.7%
Enterococcus fecium	1	1.7%
Viridians Group Streptococcus	3	4.9%
Klebsiella pneumoniae	1	1.7%
Pseudomonas aeruginosa	1	1.7%
No organism isolated	**43**	**71.7%**
Total	**60**	**100%**

Staphylococcus aureus[7 Cases]was the most common reported organism in our study 11.6% of all admitted cases .

Of this 5 cases were reported as MRSA .

The next common organism was Enterococcus species 8.3% of all admitted cases .Viridans Group Streptococci only 5% of all cases and

Gram Negative organisms attribute around 3.5% of all admitted cases

Table 17. Antibiotic sensitivity pattern: [In percentage %]

Staphylococcus spp:

Organism	Pen %	Gen %	Ery %	Clin %	CoT %	Cip %	CK %	Tet %	Van [MIC] %	Lz %	Rif %
Staphylococcus aureus MRSA[5]	0	60	0	0	0	80	60	80	100	100	100
Staphylococcus aureus MSSA[2]	100	50	50	50	0	50	0	50	100	100	100

Vancomycin and Linezolid and Rifampin were 100% sensitive.Ciprofloxacin and Tetracycline is sensitive in 80% of MRSA .

Enterococcus species

Organism	Amp %	HLG %	Ery %	CK %	Van %	Lz %	Rif %
E .faecalis[4]	50	50	25	75	100	100	100
E .fecium[1]	0	0	0	100	100	0	100

Vancomycin and Linezolid and Rifampin were 100% sensitive to E.faecalis but Vancomycin, Chloromphenicol and Rifampin were 100 % sensitive to E.fecium

Viridians Group Streptococci:

Organism	Pen [MIC] %	CTR %	Ery %	Clin %	OF %	CK %	Tet %	Van %	Lz %
Viridians Group streptococci[3]	66	100	66	66	33	100	33	100	100

VGS are 100 % sensitive to Chloromphenicol, vancomycin Ceftriaxone and Linezolid

Klebsiella pneumoniae:

Organism	AK %	Gen%	CTR %	CoT %	CK %	Tet %	Cip %	Mer %	PT %
Klebsiella pneumoniae[1]	100	100	100	0	0	100	0	100	100

K.pneumoniae was 100% sensitive to Tetracycline, Meropenem Ceftriaxone Amikacin and Gentamycin

Pseudomonas aeruginosa:

Organism	AK %	Gen %	Cip %	CTZ %	PT %	Mer %
Pseudomonas aeruginosa[1]	100	0	0	100	100	100

P.aeruginosa were 100% sensitive to Meropenem ,PiperacillinTazobactum and Ceftazidime and Amikacin.

Table 18. Analysis of patients in our study with respect to Culture positivity and Culture negativity

Variables	Culture positive [17]	Culture negative[43]	P value
Age			
18-30	5 [**29.4%**]	18 [**41.9%**]	NS
31-40	7 [**41.2%**]	9 [**20.9%**]	NS
41-50	5 [**29.4%**]	8 [**18.6%**]	NS
51-60	0	2 [**4.7%**]	
>60	0	6 [**14%**]	
Sex			
Male	9 [**52.9%**]	24 [**55.8%**]	NS
Female	8 [**47.1%**]	19 [**44.2%**]	NS
Underlying heart disease			
RHD	11 (**64.70%**)	25 (**58.1%**)	NS
CHD	1 (**5.9%**)	8 (**18.6%**)	NS
CAD	1 (**5.9%**)	3 (**7 %**)	NS
No previous heart disease	4 (**23.5%**)	7 (**16.3%**)	NS
Prior Antibitic Therapy	3 (**17.6 %**)	32 (**74.41%**)	p<0.001
COMPLICATION			
CCF 23	11 **[64.70%]**	12 [**27.9%**]	p<0.017
Stroke 9	5 **[29.41%]**	4 [**9.3%**]	NS
Renal failure 6	2 [**11.76%**]	4 [**9.3%**]	NS
Septic shock 2	2 [**11.76%**]	0	
OUTCOME			
Recovered 37	11 [**64.7%**]	26 [**60.5%**]	NS
Not recovered 11	5 [**29.4%**]	6 [**14%**]	NS
LOST FOLLOW UP 12	1 [**5.9%**]	11 [2**5. 5%**]	NS
Left side IE 50 [excluding2 tricuspid, and1 device in Rt .ventricle and no vegetation in 7 cases]	**17**	**33**	

Table19. Risk factor analysis of OUTCOME of 60 patients

Characters	***Recovered***	***Not recovered***	***Not on follow up***
Male [33]	19	7	7
Female [27]	17	4	6
RHD [36]	**21**	**9**	**6**
CHD [9]	**5**	**1**	**3**
Degenerative cardiac disease[4]	**4**	**0**	**0**
No underlying heart disease previously known[11]	**7**	**2**	**2**
Native valve IE [46]	31	7	8
Prosthetic IE [13]	5	4	4
Intra cardiac Device[1]	1	0	0
Culture positiveIE [17]	**11**	**5**	**1**
Culture negative [43]	**26**	**6**	**11**
Left sided [excluding2 tricuspid and1 device in Rt .ventricle and no vegetation in 7 cases] [50]	30	11	9

Discussion

DISCUSSION

We analysed our study results with various studies done on InfectiveEndocarditis in India in recent and past 4 decades and also compared with Western study Reports in the following factors including Demographics, Predisposing underlying heart disease, Clinical features, Co-Morbid conditions , Blood culture Results , Echocardiographic findings like vegetation, Line of Management and Outcome and tried to find the important changes in clinical, microbiological pattern of infective Endocarditis in our region.

60 patients were admitted in our tertiary care centre were diagnosed as having IE episode during this study period .Modified Dukes criteria was used in diagnosis of IE, 37 patients were labeled Definite IE[62%] cases and 23 were labeled as Possible cases[38%], which was closely similar to the study done by Ashish Gupta et al and who reported 74% of definite IE and 26 % possible IE [21]

In our study out of 60 cases , 77% cases had native valve Endocarditis [NVE] and 21.3 % had prosthetic valve Endocarditis [PVE] and 1.7% were intra cardiac device associated IE which is closely similar to study done by Ashish Gupta et al[2004 to 2009] who reported 68% of NVE and 32 % of PVE [21]

Demography:

Majority of our patients presented in the mean age 37.25±14.23, which is contrary to earlier Indian studies [mean age around 27]and the study reported by Ashish Gupta et al[2004 -2009] who reported mean age 49±13.7 but comparable to the recent study reported by Abhilash et al [2005-2015] at Vellore (41.8 ± 14.2)

The factors contributed to higher age group in our study are due to increase in age of general population as a whole in the study conducted area.

The EHS [European Heart Survey] study done in Western countries [2001] reported mean age at presenting IE was 56 ±17 which is totally reflecting modern era of developed countries[17]. But in a five year study conducted in Pakistan 1997 to 2001 reported that mean age at the time ofpresentation were 29 only [56]

There is no significant preponderance related to sex variable in our study . Male : Female ratio was 1.2:1.0 which is entirely different from recent studies reported by Abhilash et al (3.6:1) and Senthil Kumar et al (2.3 :1) and Ashish Gupta et al [3.3 :1] [21 &33&22]

The selection of patient in our study is unbiased and this demographic factor should be resulted fromthe increased awareness of seeking medical aid in female gender also in our region.

PREDISPOSING UNDERLYING HEART DISEASE :

More than three fourth (81.6 %) the patients were already diagnosed to have predisposing underlying heart disease s prior to the onset of this IE episode.

Rheumatic heart disease [RHD] was the most predominant underlying heart disease identified among the IE patients in our study predisposing to 60 % of all IE cases while congenital heart disease [CHD] predispose to 15 % of all IE in our study.

18.4 % patients were asymptomatic before the present episodes of Infective Endocarditis and they were determined to have RHD finally. This data regarding RHD as a major predisposing factor is higher than the other recent reported studies , Abhilash et al reported 40.6%, N Garg et al reported 46.9%.[21 &22&33]

Indian council of Medical Research shows the prevalence of RHD be 2.97/ 1000 in 1992 -95 and 0.9/1000 in 2002-2005, based on school survey [22] but still the prevalence of RHD have been implicated as

important predisposing heart disease for IE particularly in South India. The overcrowding and increased medical facility available to diagnose rheumatic fever in our region might be the reason for the increased report of RHD in our study. The congenital heart disease predispose of 15% of IE episodes in our study which are lower than the other studies reported by N Garg et al (28.6%) AshishGupta et al (23%) but comparable to Abhilash et al (13.9%) . The exclusion of patients age below 18 years might be reason for this result.

Mitral valve heart disease was predominant in RHD [48.3% cases] and Rheumatic Aortic valve disease were 11.6% which were comparable to the study reported by N.Garg et al (Mitral valve disease -42% and Aortic valve -7%)

Among the CHD, VSD was predominant cardiac lesion and Bicuspid aortic valve seconds to it which are comparable to S R Jain et al.[32]

The prosthetic valve was involved in 21.3% of all IE cases reported in contrary to study reported by Abhilash et al[10%] and Senthilkumar et al reported 4.3% at Chennai in 2010 and Ashish Gupta et al , New Delhi reported 31%. .[22& 21& 33]

The reasons for increased PVE are due to increased cardiac surgery for rheumatic heart disease which is also high prevalence in our region

comparing to other studies. Increased cardiac surgeries performed during last 8 years in Chennai than previous study period by Senthilkumar et al, might also be a reason .

Regarding the portal of entry, we are able to identify portal of entry in 5 patients of our study (10%) which is comparable to Abhilash et al (15.5%).

CLINICAL FEATURES AND COMORBITIDIES

Fever was the most common presenting feature [98%] which is comparable to almost all studies reported on IE. [Sharad R Jain et al reported 96% Senthilkumar et al reported 92%].The mean duration of fever was 22.3 ±8.28 days. Anaemia was reported in 21.6% cases. 15% of patients in our study was presented with infarct and embolic manifestations which is comparable to Ashish Gupta et al who reported 11 % [21]. Increased awareness of cardiological status screening in stroke ward patients in our tertiary care centre may be the reason for detecting IE in patients admitted for neurological symptoms and signs.

10% of patients in our study had chronic renal failure as a co morbid condition on regular dialysis (home/hospital)which is comparable to Abhilash et al (reported 10%). This co-morbid conditions gives the higher

yield of Health care associated IE which is 21.6% in our study is comparable to study done by OslanFrancishetto et al [58]

IMPORTANCE OF ECHOCARDIGRAM:

In our study Trans Thoracic Echocardiogarphy [TTE]was done in all cases and detected Vegetation/related findings in 51 cases and Trans Eosophageal Echo [TEE] detected additional 2 cases. Echo positivity was 88.3% in our study which is comparable to study reported by N Garg et al [89.9%] and AshishGupta et al [88%.].

In PVE, TTE diagnosed 61% cases of vegetation which is in near close to the study by Abhilash et al who reported TTE detection sensitivity was 50% only in PVE cases .

Mitral valve [56.6%]and aortic valve [26.6%] were the most commonly affected valves in our study similar to the study reported by Abhilash et al (Mitral valve -52.9% and Aortic valve - 23.2%) and Senthil Kumar et al (Mitral- 57.1%and Aortic -41.8%) and N Garg et al [Mitral valve -36% and Aortic valve - 34.8%] which show the valve affected in IE is showing no significant change since past 3 decades. [22&33]

COMPLICATIONS

CCF was the commonest complication in our study[38%]in similar to N Garg et al[41%]and S R Jain et al [42%] but different from Abhilash et al 21.5%.[22&21&32*]

The next common complication was stroke [15%] in our study which is comparable to 11% in a study reported by Ashish Gupta et al and 15% by Tariq et al, 16.5% by N.Garg et al, reflecting the neurological complications remains same for past 2 decades. But improved utility of Echo screening in patients admitted in stroke wards will increase the probability of Endocarditis detection in near future.

Septic shock was associated in 2 cases [3.2%]which is comparable to the study by Tariq et al 4% but differs from 11% reported by Abhilash et al. [21 & 22.]

The renal impairment was worsened in all the 6 cases of CRF and renal parameters elevated more during this illness which may be due to the underlying sepsis .

BLOOD CULTURE RESULT

Among 60 patients admitted for infective Endocarditis ,the culture positivity is only 28.3% which is in between the recent study reported by Senthilkumar et al [23.3%] and by S R Jain et al [40%] but other studies

done in this IE in India reported blood culture positivity as 47% by Choudhury et al and 67% by N Garg et al .The recent study reported by Abhilash et al at Vellore reported 83.7% culture positivity where he used automated methods for detection of culture which is reflecting the same result reported in western countries.[23]

The reason for this low culture positivity might be due to prior misuse of antibiotic therapy started by referring physicians well before the determination of Endocarditis as the diagnosis , prior to the admission in this tertiary care hospital.

In our study of the 43 patients who were reported culture negative, around 75% received prior antibiotic therapy within 2 weeks before this admission which is significant and comparable to the study reported by Senthilkumar et al 76% and N garg et al who reported 78%.

The commonest organism reported in our study was staphylococcus aureus 11.6% which is comparable to the study by S R Jain et al[32]who reported staphylococci16% as the predominant organism followed by the streptococci species 12% .

Enterococcus species were reported around 8.3 % in our study which is comparable to study reported by Abhilash et al [9.8%% cases of Enterococcus species causing IE] and N Garg et al who reported 8.1% as

Enterococcus. The rising prevalence of Enterococcus species may be due to increased reports of health care associated infections and increased incidence of gastrointestinal surgeries and diagnostic measures in recent years . The Viridans Group Streptococci accounts only 5 % of all our cases which is very low in comparing to studies reported by Abhilash et al[44%]and N Garg et al [23.2%].Prior empirical therapy with pencillin and related antibiotic use by the referring doctors might be the reason for this .

MANAGEMENT

Out of 60 patients around 9% cases were treated by surgical line of management [1 case -Refractory CCF and 2 cases - Prosthetic Para valvular leak and 1 case Periannular abscess and 1 case Chordae structure rupture during the hospital stay] which is close to Tariq et al who reported 11% and Abilash et al 15% cases. All the cases underwent surgical line of management were not recovered . The remaining 55 cases were treated by medical line of management. Of this 6 cases (including those who went against medical advice due to poor prognosis) were determined as not recovered and 12 cases lost follow up.

The in hospital mortality was around 18% which is comparable to Abhilash et al [23.8%] N.Garg et al[21%] and 26%by Math et al(2000 to 2004) . 20% cases werelost follow up in our study . Overall recovery rate in our study was 62%.

Regarding the cause of death, it was thought to be refractory CCF was prime cause of death[55%]which is comparable to Abhilash et al who reported 58.5% in his study .Septic shock causing mortality in 18% of cases and stroke complicated IE accounts 18% mortality .

Regarding the PVE , 30%PVE cases were not recovered and 30% of PVE cases lost their follow up and 40% of cases were improved.

Summary

SUMMARY

77%NVE and 21.3%PVE were reported in our study.

RHD still be the predominant underlying heart disease in our study.

Mitral valve was the most commonly affected valve .

TTE plus TEE [61%+16%]detection sensitivity in PVE were 77% and TTE detection sensitivity in all IE cases was 88% which was **significant** in our study.

Culture positivity was 27.3% only.

CCF was the most common complication reported in culture positive cases and commonest cause of mortality in our study which **is significant**.

Around two third of cases were recovered from the illness in our study which is **significant.**

Staphylococcus aureus was the most common causative organism reported in our study.

Culture negativity due to prior antibiotic treatment before admission in our centre were reported as around 75% which is **significant** in our study.

Conclusion

CONCLUSION

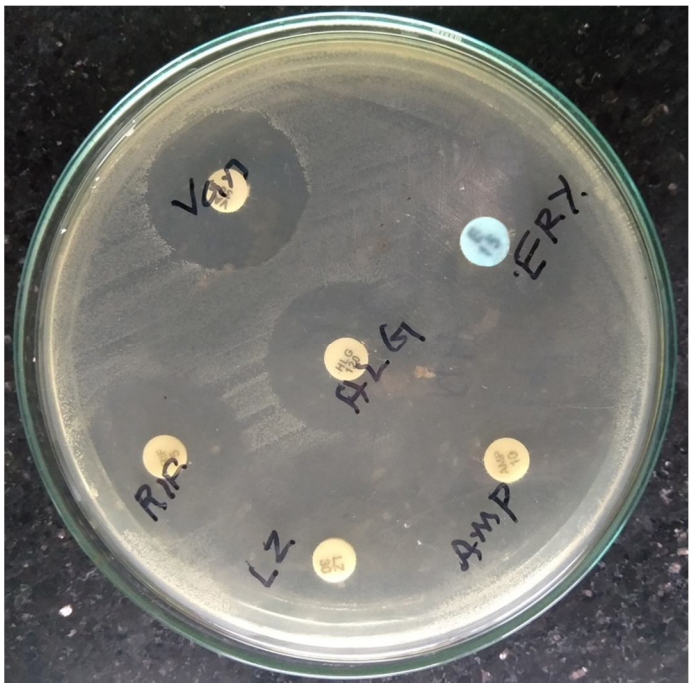
Over the past 5 decades in spite of modern techniques and methods in diagnostic field and improved medical and surgical interventions in this modern medical era , the overall mortality due to Infective Endocarditis , remains the same 25-40%.[44]

The Increased Health care associated infections in recent years made significant change in the profile of causative organisms pattern particularly the emergence of Staphylococcus as the most common etiological organism followed by Enterococcus spp .

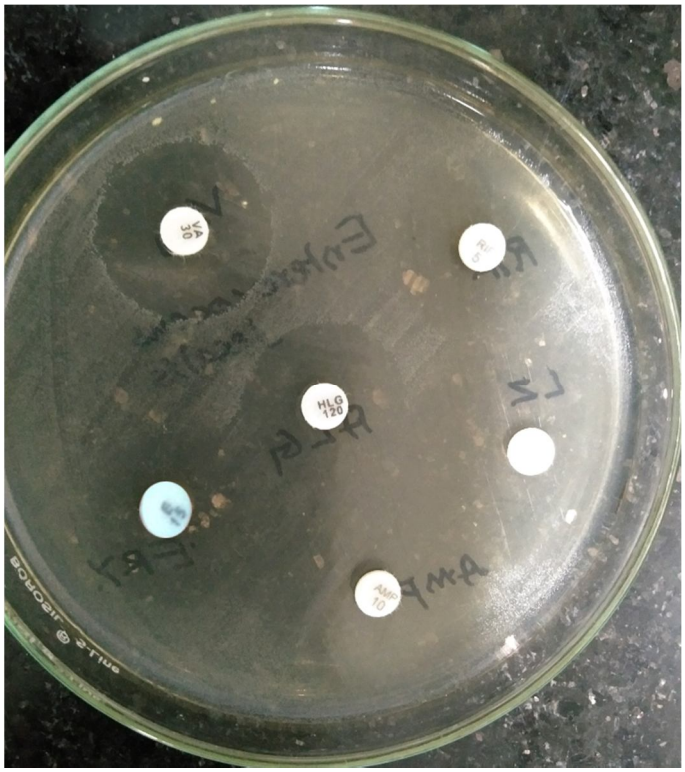
RHD still be the common predisposing underlying heart disease to cause IE in India.

The culture positivity is still lower in developing countries like India compared to western countries .The need of awareness in treating physicians in primary and secondary care centres to **adhere to practice atleast one blood culture investigation prior to empirical antibiotics** while treating suspected Infective Endocarditis patients , will improve not only the culture positivity but also proper selection of antibiotic to treat the illness and there by reduce the mortality by Infective Endocarditis .

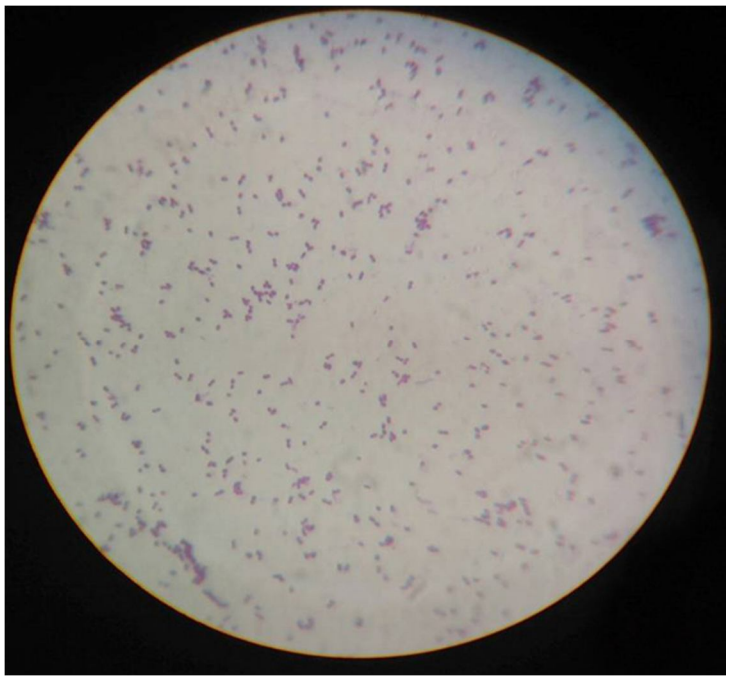
Colour Plates



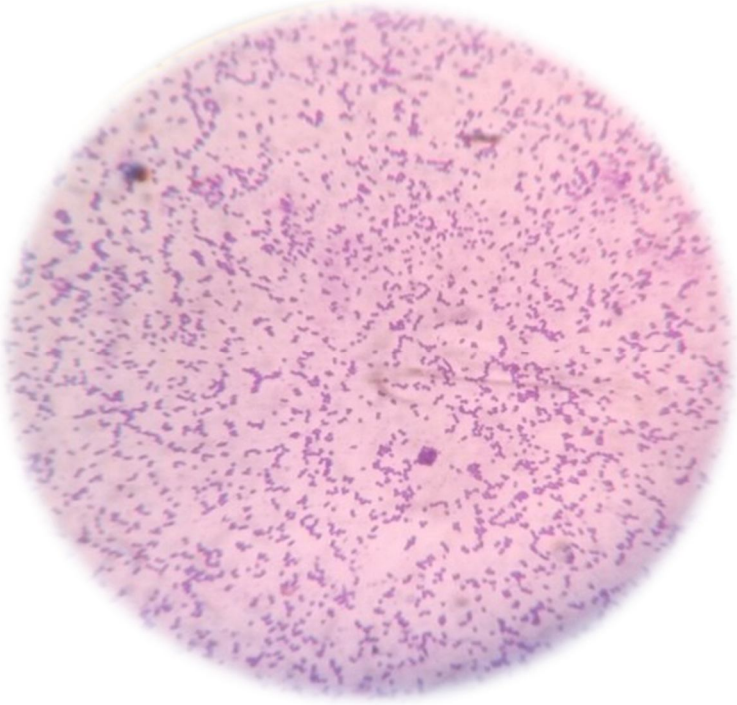
1.Enterococcus faecalis



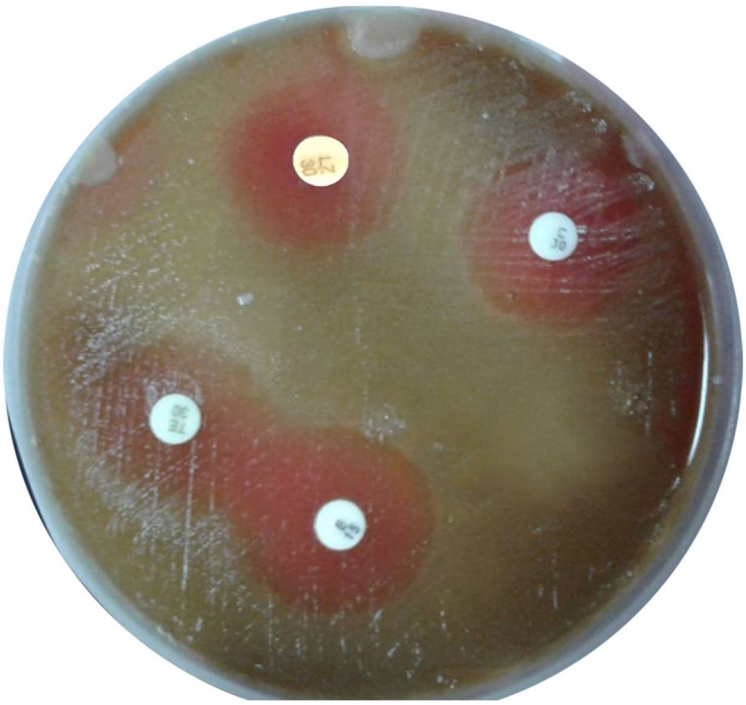
2.Enterococcus



3.GPC in pairs

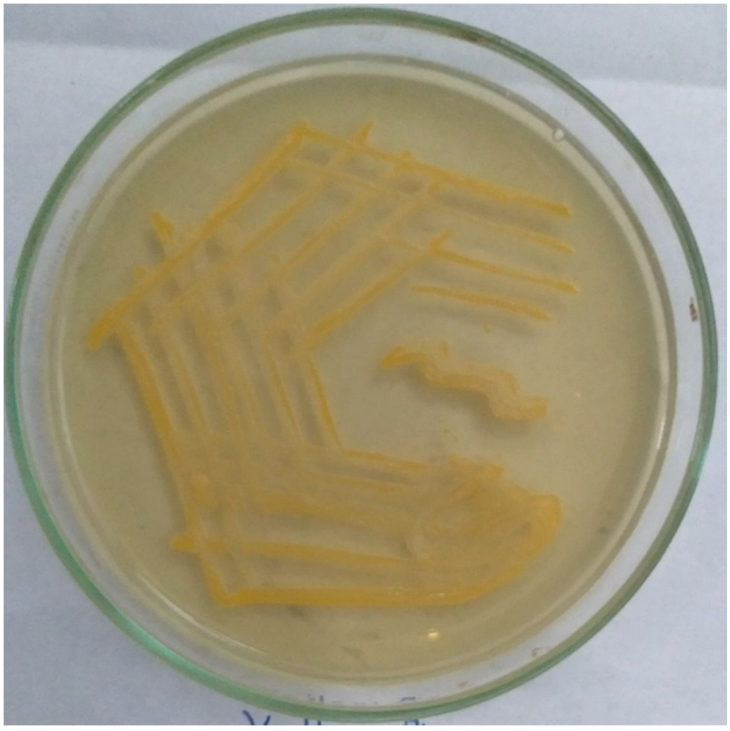


4. GPC in long chains



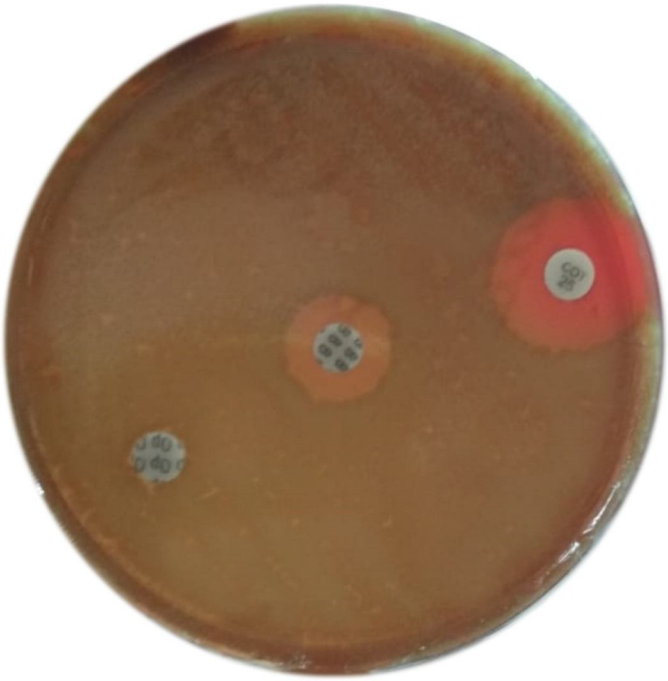
5. Alpha Hemolytic Colonies

6a. MIC for Vancomycin in S.aureus

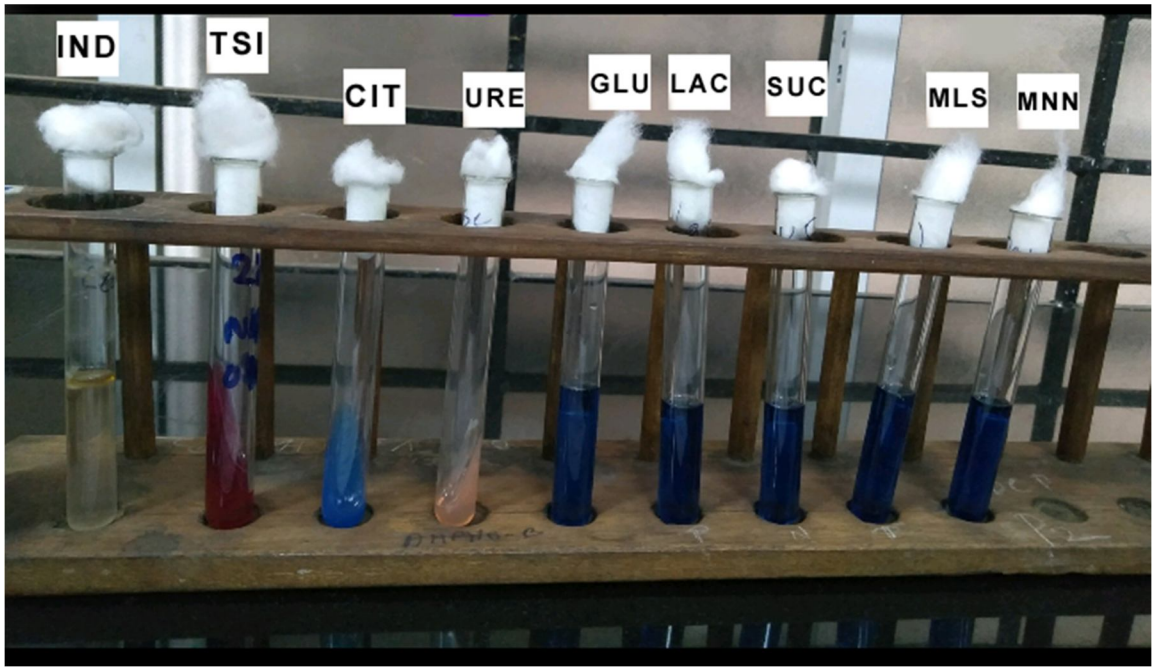


6b. Yellow Colour S.aureus

7. MIC for Vancomycin in Enterococcus



8. Optochin resistance VGS



9. Biochemical reaction of pseudomonas

10. Biochemical reaction of K.pneumoniae

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Annexures

APPENDIX-1

ABBREVIATIONS

IE	-	Infective Endocarditis
PVE	-	Prosthetic valve Endocarditis
NVE	-	Native valve Endocarditis
RHD	-	Rheumatic heart disease
CHD	-	Congenital heart disease
CAD	-	Coronary artery disease
AML	-	Anterior mitral leaflet
PML	-	Posterior mitral leaflet
RCC	-	Right coronary cusp
LCC	-	Left coronary cusp
CC	-	Non coronary cusp
VSD	-	Ventricular septal defect
CNIE	-	Culture negative Infective Endocarditis
CPIE	-	Culture positive Infective Endocarditis
TTE	-	Trans thoracic echocardiography
TEE	-	Trans esophageal echocardiography
CCF	-	Congestive cardiac failure
CRF	-	Chronic renal failure

ANNEXURE – I

INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.T.Kannan
I Year PG in MD Microbiology
Institute of Microbiology
Madras Medical College
Chennai 600 003

Dear Dr.T.Kannan,

The Institutional Ethics Committee has considered your request and approved your study titled **"A STUDY ON BACTERIOLOGICAL PROFILE OF INFECTIVE ENDOCARDITIS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL" - NO.06032017(I)**

The following members of Ethics Committee were present in the meeting hold on **02.03.2017** conducted at Madras Medical College, Chennai 3

1.Dr.C.Rajendran, MD.,	:Chairperson
2.Dr. K.Narayanasamy,MD,DM.,Dean(FAC), MMC,Ch-3	:Deputy Chairperson
3.Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3	: Member Secretary
4.Prof.S.Suresh, MS, Prof. of Surgery,MMC,Ch-3	: Member
5.Prof.Baby Vasumathi,MD.,Director, Inst. of O & G	: Member
6.Prof.K.Ramadevi,MD.,Director,Inst.of Bio-Che,MMC,Ch-3	: Member
7.Prof.R.Padmavathy, MD, Director,Inst.of Pathology,MMC,Ch-3	: Member
8.Tmt.J.Rajalakshmi, JAO,MMC, Ch-3	: Lay Person
9.Thiru S.Govindasamy, BA.,BL,High Court,Chennai	: Lawyer
10.Tmt.Arnold Saulina, MA.,MSW.,	:Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE
CHENNAI-600 003

APPENDIX-II

A).STAINS AND REAGENTS

Gram staining:

- Methyl violet(2%)-10g of Methyl violet in 100 ml Absolute alcohol in 1 litre of Distilled water.(primary stain)
- Grams Iodine-10g Iodine in 20 g KI(fixative)
- Acetone-Decolourizing agent.
- Carbol fuchsin(1%)-Secondary stain.

MEDIA USED

MacConkey agar medium
Composition

Ingredients gram/liter

- Peptone 20g
- Lactose 10g
- NaCl 5.g
- sodium deoxycholate 1.0
- Neutral Red 0.03
- Agar 15.0

Fifty-two grams of dehydrated MacConkey agar medium was suspended in 1000 ml colddistilled water and boiled to dissolve the medium completely. The solution was thensterilized by autoclaving at 121°C and 15 lbs pressure for 15 minutes.

Blood agar medium(5% sheep blood agar)
Composition

Ingredients gram/liter

Peptone 10.00
Distilled water 1 ltr.
Sodium chloride 5.00
Agar 15.00

Forty grams of the dehydrated blood agar medium was suspended in 1000 ml cold distilled water in a flask and boiled to dissolve the medium completely. It was thensterilized by autoclaving at 121^0 C and 15 lbs pressure for 15 minutes. The autoclavedmaterials were allowed to cool to a temperature of 45^0C in a water bath. Defibrinated5-10% sheep blood was then added to the medium aseptically and distributed to sterile petri dishes. Sterile media was stored in refrigerator at 40C for future use.

Muller Hinton agar medium
Composition

Ingredients gram/liter

Beef dehytrated infusion 300
Casein hydrolysate 17.50
Starch agar 1.50
Agar 10.00

Thirty-eight grams of dehydrated Mueller Hinton agar medium was suspended in1000 ml cold distilled water and boiled to dissolve the medium completely. The solutionwas then sterilized by autoclaving at 121°C and 15 lbs pressure for 15 minutes. Theautoclaved media was stored at 4°C.pH=7.4

MEDIA REQUIRED FOR BIOCHEMICAL IDENTIFICATION:
Catalase test: 3% hydrogen peroxide

Oxidase reagent

Composition
Distilled water 10ml
Tetramethyl-P- phenylenediminedihydrochloride 0.1 g

Indole test
Composition
Ingredients amount

Peptone 20g
Sodium chloride 5g
Distilled water 1 L
After adjustment of the pH to 7.4 , sterilize by autoclaving at 1210C for 15 min.
Kovac.s reagent
Amyl or isoamyle alcohol 150ml
p . Dimethyl-aminobenzaldehyde 10g
Hydrochloric acid 50ml
Dissolve the aldehyde in the alcohol and slowly add the acid and store in therefrigerator.

Simmon's Citrate Medium:

- Koser's medium 1 ltr
- Agar 20g
- Bromothymol blue 0.2% 40ml
- Dispense,Autoclave at 121°for 15 min and allow to set as slopes.

Triple Sugar Iron medium:

- Beef extract 3g
- Yeast extract 3g
- Peptone 20g
- Glucose 1g
- Lactose 10g
- Sucrose 10g
- Ferric citrate 0.3g
- Sodium chloride 5g
- Sodium thiosulphate 0.3g
- Agar 12g
- Phenol red 0.2% solution 12 ml
- Distilled water 1 ltr

Heat to dissolve the solids,add the indicator solution,mix and tube .Sterilize at 121° for15 min and cool to form slopes with deep butts.

Methyl Red test/Voges –Proskauer test:

A.MR/VP broth(Glucose broth/phosphate buffer broth)

Polypeptone 7g
Glucose 5g
Dipotassium phosphate 5g
Distilled water 1Ltr
Final pH 6.9

B.Reagents for GNB

1 alpha -Napthol,5%(5gm in 100ml of absolute ethyl alcohol)
2.Potassium hydroxide 40%(Potassium hydroxide in 100ml of Distilled water).

Decarboxylase media:

Moller decarboxylase broth base:

Ingredients gms/ml
Peptone 5
Beef extract 5
Bromocresol purple 0.01
Cresol red 0.005
Glucose 0.5
Pyridoxal 0.005
Aminoacid
Add 10g of the levo form of the aminoacid for 1000 ml.mix and dispense in sterile tubes.

Hugh-Leifson's Oxidation-Fermentation test:

Peptone 2g
Sodium chloride 5g
D-glucose 10g
Bromothymol blue 0.03g
Agar 3g
Dipotassium phosphate 0.3g
Distilled water 1ltr
pH=7.1
Basal medium is autoclaved.1%of sterile sugar solutions is added to the basal medium.Dispense into the sterile test tubes without slant.

McFarland Standard 0.5

Composition and preparation 1 % (V/V) solution of chemically pure (0.36N) Sulphuricacid and 1.175 % (W/V) solution of chemically pure (0.048M) barium chloride wasprepared in two separate sterile flasks. Then 9.9 ml of sulphuric acid and o.1 ml ofbarium chloride were added to the clean screw capped test tube and sealed. The bariumsulphate suspension corresponds approximately to McFarland standard tube No.1 withcorresponding cell density of 3 × 108 organisms/ml. To made the turbidity standard ofcell density to one half of the McFarland standard tube No.1 which correspond to celldensity of 1.5 × 108 organism/ml for determination of antibiotic sensitivity by Kirby-Bauer inoculated technique 0.5 ml of 1.7 %(W/V) barium chloride (Bacl2 2H2O) wasadded to 99.5 ml of 1 % (V/V) Sulphuric acid (0.36N), mixed well and 5- 10 ml wasdistributed in sterile capped test tubes and sealed.

PROFORMA

- Name : IP NO:
- Age: Ward:
- Sex:
- Occupation:
- Address:

- Presenting complaints:
- Signs observed in patient:

- Personal history:

- Past history:
- Past treatment history:

- Previous echo diagnosis:

- Now clinical diagnosis:
- Present echo findings:
- Other lab investigations:

- Microbiological investigation:
- Direct Gram staining :

- Culture : 1 2 3

  Blood agar

  Chocolate agar

  Mac Conkey agar

- Organism identified:
- Antimicrobial sensitivity pattern:

CONSENT FORM

STUDY TITLE:

"A STUDY ON BACTERIOLOGICAL PROFILE OF INFECTIVE ENDOCARDITIS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL".

I……, hereby give consent to participate in the study conducted by Dr T.KANNAN, Post graduate at Institute of Microbiology, Madras Medical College, Chennai and to use my personal clinical data and the result of investigations for the purpose of analysis and to study the nature of the disease, I also give consent to give my clinical Specimen (blood) for further investigations.I also learn that there is no additional risk in this study. I also give my consent for my investigator to publish the data in any forum or journal.

Signature/ Thumb impression Of the patient/ relative Place Date

Patient Name & Address:

Signature of the Investigator:

Signature of Guide:

INFORMATION SHEET

STUDY TITLE :

"A STUDY ON BACTERIOLOGICAL PROFILE OF INFECTIVE ENDOCARDITIS IN PATIENTS ADMITTED IN A TERTIARY CARE HOSPITAL"

INVESTIGATOR : **Dr T.KANNAN,**
Post Graduate,
Institute of Microbiology,
Madras Medical College,
Chennai – 600003.

GUIDE : **Dr.J.EUPHRASIA LATHA.M.D.,**
Director i/c&Professor of Microbiology,
Institute of Microbiology,
Madras Medical College,
Chennai – 600003.

Infective Endocarditis is caused by microbial infections mostly involves heart valves (native or prosthetic) but may also occur on low pressure side of a ventricular septal defect, on mural endocardium damaged by aberrant jet of blood or foreign bodies or on intracardiac devices themselves.

In Infective Endocarditis , Isolation of causative organism from blood culture is critical for diagnosis and planning treatment. Patients included in this study after getting informed consent only. This study is entirely voluntary and patient can withdraw any time from this study. Extra cost will not be incurred to the patients in this study. Any doubt regarding this study will be willingly clarified. Results of the study will be published. In case of any doubt please contact Dr. T.KANNAN, Cell: 9965797305.

MASTER CHART

IP NUMBER	AGE	SEX	UNDERLYING HEART DISEASE ALREADY KNOWN	FEVER DURATION	CLINICAL FEATURES	COMORBID CONDITION	ECHOCARDIGRAPHIC FINDINGS	BLOOD CULTURE RESULT	NUMBER OF POSITIVE CULTURES	NVE/PVE /Device associated IE	VALVE INVOLVED IN VEGETATION -M/A/T/P	ORGANISM ISOLATED
58772	25	F	RHD	25 DAYS	chestpain, arthralgia,	NIL	VEGETATION ON MITRAL VALVE PML[posterior mitral leaflet]	POSITIVE	3	NATIVE	MITRAL	Enterococcus faecalis
51416	40	F	RHD	12 DAYS	chestpain,splenomegaly,,,pedal edema,arthritis,elevatedjvp,	SEIZURE DISORDER	VEGETATION ATTACHED TO PML MITRAL VALVE	POSITIVE	2	NATIVE	MITRAL	Viridans Group Streptococci -Mitis group
55136	47	M	NOT	15 DAYS	pedal edema,dyspnoea,chestpain,pallor,jvp raised	Chronic Renal Failure-RENAL TRANSPLANTATION DONE . SYS.HT	vegetation present Non coronary cusp[NCC] of AORTIC valve	POSITIVE	2	NATIVE	AORTIC	Viridans Group Streptococci species - Mitis group
58895	47	M	NOT	14 days	splenomeagaly hepatomegaly,chestpain, ,clubbing,jaundice,pallor,palpitation,janewa y lesions	CHRONIC LIVER DISEASE [HBsAgPOSITIVE] ,DIABETES	VEGETATION motile mass attached to AML -MITRAL VALVE, Moderate MR	POSITIVE	1	NATIVE	MITRAL	Staphylococcus aureus-MRSA
60522	32	F	RHD	20 DAYS	dyspnoea,splenomegaly,clubbing,petechiae jvp raised,pedal edema	DIABETES ,HYPOTHYRIOD	VEGETATION attached to AML-MITRAL VALVE,MR MODERATE	POSITIVE	2	NATIVE	MITRAL	Staphylococcus aureus-MRSA
70806	19	F	CHD -VSD	11DAYS	splenomegaly,palpitation,pallor	NIL	vegetation at Right coronary cusp[RCC] of AORTICVALVE. No shunt across VSD	POSITIVE	2	NATIVE	AORTIC	Pseudomonas aeruginosa
67764	20	M	RHD	17DAYS	chestpain,palpitation,pallor, sub conjuctival hemorrhages ,petechial skin lesions	NIL	vegetation attached to NCC of AORTIC VALVE	NEGATIVE	0	NATIVE	AORTIC	No organism
62352	32	M	NOT	32 DAYS	dyspnoea,splenomegaly,clubbing,pedal edemapalpitationk/c of membranous nephropathyloa,low	CHRONIC RENAL FAILURE. SYS. HT	vegetation >10mmin size attached to RCC of AORTIC VALVE .moderate AR	POSITIVE	3	NATIVE	AORTIC	Enterococcus fecium
97623	28	F	RHD	45 days	arthralgia,clubbing,splenomegaly,	NIL	VEGETATION attached to PML-MITRAL VALVE,Modearte MR	POSITIVE	1	NATIVE	MITRAL	Enterococcus faecalis
87641	35	M	RHD	15 DAYS	splenomegaly,dyspnoea,oslers nodes,arthralgia,pedal edema,chestpain jvp raised	NIL	VEGETATION attached to PML-MITRAL VALVE,Modearte MR	POSITIVE	1	NATIVE	MITRAL	Staphylococcus aureus-MSSA
119944	47	M	CAD	20 DAYS	recent cerebrovascular acident [CVA]-50 days back,,residual hemiparesis. CT brain left.frontal infarct	RESIDUAL HEMIPARESIS. SYS.HT	vegetation . attached to RCC of AORTIC VALVE	POSITIVE	2	NATIVE	AORTIC	Enterococcus faecalis
102536	38	F	RHD	21 DAYS	chestpain severe aneamia,jointpain,palpitation,skinpetechiae	NIL	SEVERE MS-MR. NO vegetation	NEGATIVE	0	NATIVE	NO	No organism
85962	46	F	NOT	8 days	rthemiparesis [stroke cva],splenomegaly,altered sensorium,	HEMIPARESIS	vegetation attached to left coronary cusp[LCC] of AORTIC VALVE,moderate AR	POSITIVE	2	NATIVE	AORTIC	Staphylococcus aureus-MRSA
58579	37	M	RHD	-	rt hemiparesis,	HEMIPARESIS . ALCOHOLIC	VEGETATION motile oscillating mass attached to AML-MITRAL VALVE,severe MR	POSITIVE	1	NATIVE	MITRAL	Enterococcus faecalis
62865	20	M	RHD	30 DAYS	,splenomegay,,chestpain.clubbing,	NIL	multiple VEGATATION attached to PML-MITRAL VALVE.severe MR	NEGATIVE	0	NATIVE	MITRAL	No organism

IP NUMBER	AGE	SEX	UNDERLYING HEART DISEASE ALREADY KNOWN	FEVER DURATION	CLINICAL FEATURES	COMORBID CONDITION	ECHOCARDIGRAPHIC FINDINGS	BLOOD CULTURE RESULT	NUMBER OF POSITIVE CULTURES	NVE/PVE /Device associated IE	VALVE INVOLVED IN VEGETATION -M/A/T/P	ORGANISM ISOLATED
50194	20	F	CHD-VSD	25 DAYS	dyspnoea,,splenomegaly,jvpraised,legedema clubbing,	NIL	vegetation attached to TRICUSBID VALVE.perimembranous VSD	NEGATIVE	0	NATIVE	TRICUSPID	No organism
75127	24	F	CHD-VSD	20 DAYS	dyspnoe,oslers node,splenomegaly ,leg edema,jvp raised	NIL	smallVSD. Vegetation on AORTIC VALVE - LCC LEAFLETS severeAR	NEGATIVE	0	NATIVE	AORTIC	No organism
78487	42	M	RHD	45 DAYS	splenomegaly,clubbing,skinpetechiae ,dyspnoea,jaundice	NIL	vegetation attached to AORTICVALVE Along LCC.moderate AR	NEGATIVE	0	NATIVE	AORTIC	No organism
73426	65	M	NOT	24 days	splenomegaly,digital gangrenedue to vascular embolic,recent CT brain left frontal hypodense lesion	SEIZURE DISORDER	multiple VEGETATION AT PML-mitral valve.moderate MR	NEGATIVE	0	NATIVE	MITRAL	No organism
46190	37	M	RHD	18 DAYS	dyspnoea ,,oslers node, splenomegaly, clubbing,	NIL	vegetation attached to PML-MITRAL VALVE initially .Then follow up ECHO show CHORDAL RUPTURE	NEGATIVE	0	NATIVE	MITRAL	No organism
30896	28	M	RHD-MVR DONE	15 DAYS	recent stroke 35 days back,residual hemiparesis CT Brain infarct+	RESIDUAL HEMIPARESIS	SEVERE MS-MR. NO vegetation	POSITIVE	1	PROSTHETIC	NO	Staphylococcus aureus-MRSA
11299	65	F	RHD-MVR DONE	17 DAYS	conjuctival hemorrage,oslernodes,splenomegaly,clubbing	NIL	moderate MR, mild PARAVALVULAR LEAK-MITRAL VALVE ,partial dehiscense of MITRAL valve	NEGATIVE	0	PROSTHETIC	MITRAL	No organism
161017	37	M	NOT	35 DAYS	clubbing, USG ABDOMEN ? Splenic abcess,loss of appetite,,loss of wieght,roths spot SNAKE BITE 45 days back	NIL	multiple VEGETATION AT AML-MITRAL VALVE.severe MR	NEGATIVE	0	NATIVE	MITRAL	No organism
41922	40	F	RHD	15 DAYS	chest pain ,arthralgia, skinpetechiae,,petechia,clubbing	NIL	VEGETATION>10 mmin size ALONG PML-MITRAL VALVE .moderate MR and AR	NEGATIVE	0	NATIVE	MITRAL	No organism
77654	42	M	CHD-BICUSPID AORTIC VALVE	28 DAYS	skin petechiaea ,,cough/k/c of ckd on treament,ESR100,CRP-positive	CHRONIC RENAL FAILURE . SYS.HT	vegetation IN AORTIC VALVE on LCC	NEGATIVE	0	NATIVE	AORTIC	No organism
84916	22	F	NOT	20 DAYS	dyspnoea,oslers node,k/c of CRF on dialysis, splenomegaly,,pallor,pedal edema,	CHRONIC RENAL FAILURE	mobile mass [VEGETATION]>10 mm in sizealong AML-MITRAL VALVE,moderate MR	NEGATIVE	0	NATIVE	MITRAL	No organism
74675	23	F	RHD	15 DAYS	CT BRAIN-left frontal infarct, RT.hemiparesis,splenomegaly,,ptechiae,pallor	HEMIPARESIS	VEGETATION ATTACHED TO AML-MITRAL ,severe MR	NEGATIVE	0	NATIVE	MITRAL	No organism
6760	25	M	RHD	26 DAYS	conj.hmrge,splenomegaly,chest pain ,palpitation,	NIL	LARGE>10mm VEGETATION in AML-MITRAL VALVE mild ,MS,moderate MR,	NEGATIVE	0	NATIVE	MITRAL	No organism
27421	44	F	CHD-VSD	20 DAYS	dyspnoea,pallor,	NIL	LARGE VSD/TR NO vegetation	NEGATIVE	0	NATIVE	NO	No organism
7582	40	M	RHD-MVP	25 DAYS	dyspnea,petechia, pedal edema ,raised jvp	NIL	oscillating mass VEGETATION attached TO PML-MITRAL VALVE ,severe MR	POSITIVE	2	NATIVE	MITRAL	Viridans Group Streptococci -Mitis group
12469	33	M	RHD	20 DAYS	dyspnoea,,oselrs node,aneamic,cough,,chestpain , palpitation	NIL	VEGETATION > 10 mm in size AT PML - MITRAL VALVE .severe MR	NEGATIVE	0	NATIVE	MITRAL	No organism
8005	30	F	RHD-MVR DONE	18 DAYS	splenomegaly ,dyspnoea,	NIL	normal prosthetic mitral valve . No vegetation	NEGATIVE	0	PROSTHETIC	NO	No organism

IP NUMBER	AGE	SEX	UNDERLYING HEART DISEASE ALREADY KNOWN	FEVER DURATION	CLINICAL FEATURES	COMORBID CONDITION	ECHOCARDIGRAPHIC FINDINGS	BLOOD CULTURE RESULT	NUMBER OF POSITIVE CULTURES	NVE/PVE /Device associated IE	VALVE INVOLVED IN VEGETATION -M/A/T/P	ORGANISM ISOLATED
1587	21	M	NOT	20 DAYS	CT BRAIN -left mca infarct.frontoparaital hypodense ,hemiparesis,	HEMIPARESIS	multiple VEGETATION AML -MITRAL VALVE with MR,	NEGATIVE	0	NATIVE	MITRAL	No organism
2277	50	M	RHD -AVR DONE	21 DAYS	recent stroke 40 days back ,dm on insulin,residuald mild hemiparesis,,petechiaea,	DIABETES. SYS.HT/residual HEMIPARESIS	NORMAL prostheticVALVES WITH AR. NO vegetation	POSITIVE	2	PROSTHETIC	NO	Klebsiella pneumoniae
13886	75	M	CAD .	17 DAYS	chest pain,skin petechiaea,,pacemaker done in past,splenomegaly	SYS HT	oscilatory mass ? VEGETATION in PML -MITRAL AVALVE	NEGATIVE	0	NATIVE	MITRAL	No organism
61240	27	M	CHD-VSD	21 DAYS	recent craniotomy for intra cranial abcess done ,petechiae,splenomegalyroths spot	SEIZURE DISORDER	LARGE VSD. RTCORNARY CUSP PROTRUDING INTO RVOT	NEGATIVE	0	NATIVE	NO	No organism
60414	19	M	RHD-AVR DONE	20 DAYS	conjuctival hemorrhage,petechial hemorrhage,,anemic,clubbing	NIL	vegetation ALONG AORTICVALVE ring BY TEE.	NEGATIVE	0	PROSTHETIC	AORTIC	No organism
78635	64	F	RHD-MVR DONE	18 DAYS	splenomegaly ,chest pain , arthralgia,clubbing	NIL	VEGETATION> 10 mm in size along-MITRAL VALVE ring,moderate MR	NEGATIVE	0	PROSTHETIC	MITRAL	No organism
7308	38	F	RHD	16 DAYS	clubbing,chestpain,	NIL	VEGETATION>10 mm in size in AML-MITRAL VALVE . MR	NEGATIVE	0	NATIVE	MITRAL	No organism
124325	48	M	RHD	28 DAYS	splenomegaly,skinpetechiae ,dyspnoeae , petechiaea,,anemia	NIL	TORN AMLLEAFLETSEVERE MR.TR MILD?VEGETATION along AML-MITRAL VALVE	NEGATIVE	0	NATIVE	MITRAL	No organism
86619	32	F	CHD-BICUSPID AORTIC VALVE	27 DAYS	roths spot,,splenomegaly,,anemia,chestpain petechialskin lesions,palpitation ,clubbing	CHRONIC RENAL FAILURE	Bicuspid aortic valve . NO vegetation	NEGATIVE	0	NATIVE	NO	No organism
69971	20	F	RHD -AVR DONE	21 DAYS	dyspnoea, ,petechiae, , ,anemic	NIL	vegetation>10 mm in size in prosthetic AORTIC VALVE ring	NEGATIVE	0	PROSTHETIC	AORTIC	No organism
15571	35	F	RHD-DVR DONE	18 DAYS	splenomegaly, dyspnoeae,anemic,CRP positive . procalcitonin - 6.02ng/ml. RA factornegative	NIL	TRIVAL PARAVALVULAR LEAK-MITRAL VALVE	POSITIVE	1	PROSTHETIC	MITRAL	Staphylococcus aureus-MRSA
15519	55	M	RHD -MVP	18 DAYS	chest pain ,palpitation,recent TIA, CT brain lacunar infarct- NO RESIDUAL HEMIPARESIS	SYS.HT. SEIZURE DISORDER	VEGETATIONAT PML- MITRAL VALVE . severe MR	NEGATIVE	0	NATIVE	MITRAL	No organism
17840	40	M	RHD-AVR DONE	22 DAYS	dyspnoea,pedaledema,skin petechiaea,jvpraised,clubbing	NIL	SEVEREAR,PARVALVULAR LEAK,vegetation ATTACHED TO THE AORTIC VALVE	NEGATIVE	0	PROSTHETIC	AORTIC	No organism
32071	28	F	RHD	21 DAYS	deep vein thrombosis leg,arthralgia .RECENT ENCEPHALITIS TREATED 35 DAYS BACK	NIL	VEGETATION ATTACHED TO PML-MITRAL VALVE,moderate MR	POSITIVE	2	NATIVE	MITRAL	Staphylococcus aureus-MSSA
23428	24	F	RHD-MVR DONE	17 DAYS	recent abortion 45 days back,arthritis,aneamic .	NIL	VEGETATION> 10mmin size in prosthetic MITRAL VALVE ring	NEGATIVE	0	PROSTHETIC	MITRAL	No organism

IP NUMBER	AGE	SEX	UNDERLYING HEART DISEASE ALREADY KNOWN	FEVER DURATION	CLINICAL FEATURES	COMORBID CONDITION	ECHOCARDIGRAPHIC FINDINGS	BLOOD CULTURE RESULT	NUMBER OF POSITIVE CULTURES	NVE/PVE /Device associated IE	VALVE INVOLVED IN VEGETATION -M/A/T/P	ORGANISM ISOLATED
33173	62	M	NOT	21 DAYS	splenomegaly,,dyspnoeae.anemic	SYS. HT. DIABETES	VEGETATION ATTACHED TO AML-MITRAL VALVE.SEVERE MR	NEGATIVE	0	NATIVE	MITRAL	No organism
32988	20	M	RHD -MVR DONE	45 DAYS	dyspnoea,oslers node.petechiaea.	NIL	VEGETATION ATACHED TO MITRAL VALVE RING	NEGATIVE	0	PROSTHETIC	MITRAL	No organism
40382	20	M	NOT	25 DAY	right hemiparsisis -stroke,, splenomegaly,splenomegaly, clubbing	HEMIPARESIS	vegetation attached to RCC AORTIC VALVE,moderate AR	NEGATIVE	0	NATIVE	AORTIC	No organism
43072	37	F	RHD-MVR DONE	15 DAYS	left hemiparesis - stroke ,anemia,arthralgia,loss of weight.	HYPOTHYROIDISM . HEMIPARESIS	VEGETATION attached to PROSTHETIC MITRAL VALVE ring	.NEGATIVE	0	PROSTHETIC	MITRAL	No organism
46841	47	F	NOT	21 DAYS	dyspnoea.CRP raised,splenomegaly,pedal edema,anemic,jvpraised.ESR116,WBC26700 ,CRP87	CHRONIC RENAL FAILURE	VEGETATION >10mm in size ATTACHED TO AML-MITRAL VALVE ,SEVERE MR MODERATE AR	NEGATIVE	0	NATIVE	MITRAL	No organism
44275	28	M	CHD-VSD	48 DAYS	splenomegaly ,clubbing,, palpitation,,oslers node	NIL	VEGETATION attached to anterior TRICUSPID VALVE Leaflet on right side of VSD . mild TR	NEGATIVE	0	NATIVE	TRICUSPID	No organism
47026	28	F	RHD	18 DAYS	joint pain,chestpain palpitation,dysphnoea, clubbing.	NIL	VEGETATION attached to AML MITRAL VALVE TIP,SEVERE MR	NEGATIVE	0	NATIVE	MITRAL	No organism
39920	45	M	RHD-BMV DONE	25 DAYS	dyspnoeae,sub.conj.hmrge,,petechiaea,anemic,loss of appetite.loss of wieight.	SYS.HT	vegetation attached to AORTIC VALVE ring-BY TEE	NEGATIVE	0	PROSTHETIC	AORTIC	No organism
23009	46	M	CHD-BICUSPID AORTIC VALVE-	30 DAYS	splenomegaly,petechial skin lesions, roths spot,clubbing	NIL	vegetation attached to BICUSPID AORTIC VALVE,severe AR	NEGATIVE	0	NATIVE	AORTIC	No organism
61214	54	M	RHD	30 DAYS	dyspnoea, pedal edema, jvp raised ,RH.factor 32,oslersnode,petechieae ,ASOnegative,CRP6ng/ml	SYS.HT	periannular abcess extends to root with calcified vegetation on AORTIC VALVE	NEGATIVE	0	NATIVE	AORTIC	No organism
73672	50	M	CAD	26 DAYS	,chestpain , anemic, ESR10.	SYS.HT. DIABETES	VEGETATION AML-MITRAL VALVE . moderate MR	NEGATIVE	0	NATIVE	MITRAL	No organism
11852	71	F	CAD [COMPLETE HEART BLOCK]	18 DAYS	splenomegaly,jvp raised, pedal edema, clubbing,	SYS. HT. COMPLETE HEART BLOCK	VEGETATIONattached to right side of PACEMAKER LEAD IN SITUin right ventricle	NEGATIVE	0	DEVICE	DEVICE IN RT VENTRICLE	No organism
63246	21	F	RHD	18 days	aneamic .splenomegaly,clubbing	NIL	VEGETATION AML,MODERATE MR	NEGATIVE	0	NATIVE	MITRAL	No organism

MASTER CHART

IP NUMBER	AGE	SEX	SENSITIVE TO	RESISISTANT TO	WARD	PLACE	LIVER FUNCTION TEST	RENAL FUNCTION TEST	IV DRUG ABUSERS	HEALTH CARE ASSOCIATED	COMPLICATIONS	MANAGEMENT	OUTCOME	TYPE OF IE	PRIORANTI BIOTIC TREATMENT
58772	25	F	linezolid,vancomycin ,chloromphenicol,Rifampin	ampicllin,erythromycin,high level gentamycin	121	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	DEFINITE	0
51416	40	F	chloromphenicol,ceftriaxone, oflaxacin, vancomycin,teracyclin,linezolid	erythromycin,pencillinMIC, clindamycin	CCU	CHENNAI	NORMAL	NORMAL	NO	NO	CCF.[congestive cardiac failure]	MEDICAL	IMPROVED	DEFINITE	yes
55136	47	M	pencillinMIC,vancomycin,chloromphenicol,linezolid,ceftriaxone,clindamycin, erythromycin	tetracyclin,ofloxacin	CARDIOCCU/NEPHRO	TVNMLI	NORMAL	ABNORMAL	NO	YES. [.taken inpatient treatment andout patient follow up fortransplant]	CCF+RENAL FAILURE [ACUTE ON CHRONIC]	MEDICAL	IMPROVED	DEFINITE	0
58895	47	M	vancomycin MIC ,chloromphenicol,teracycln,linezolid ,rifampin,gentamycin	pencillin,ciprofloxacin,cotrimoxazole,, erythromycin,clindamycin	111/CARDIO CCU	TVNMLI	ABNORMAL	NORMAL	YES	NO	CCF+SEPTIC SHOCK	MEDICAL	DIED	DEFINITE	0
60522	32	F	ciprofloxacin,,linezolid,vancomycinMIC,rifampin,gentamycin	pencillin,chloromphenicol,teracyclin,erythromycin,cotrimxazole, clindamycin	C3. 30-C	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	SURGICAL	DIED	DEFINTE	0
70806	19	F	amikacin,cepapherazone - sulbactum,meropenem,piperacillin - tazobacctum,ceftazidime	gentamycin,ciprofloxacin	CCU	TVNMLI	NORMAL	NORMAL	NO	NO	CCF+SEPTIC SHOCK	MEDICAL	DIED	DEFINTE	0
67764	20	M	-	-	30-D	TVNMLI	NORMAL	NORMAL	NO	NO		MEDICAL	IMPROVED	DEFINTE	yes
62352	32	M	vancomycin,rifampin,chloromphenicol	erythromycin,ampicillin, ,high level gentamycin,,linezolid	30-D	CHENNAI	NORMAL	ABNORMAL	NO	YES [On Regular dialysis and follow up]	CCF+RENAL FAILURE[ACUTE ON CHRONIC]	MEDICAL	AMA	DEFINTE	yes
97623	28	F	vancomycin,erythromycin,,linezolid,rifampin	highlevel gentamycin,chloromphenicol,ampicillin	30-C	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	DEFINTE	0
87641	35	M	pencillin,ciprofloxacin,linezolid,vancomycinMIC,rifampin,	gentamycin,erythromycin,clindamycin,teracyclin,chlorompenicol,cotrimaxazole	ICCU-CARD	TVNMLI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	DEFINTE	0
119944	47	M	vancomycin,chloromphenicol,ampicillin,Highlevel gentamycin,linezolid, rifampin	erythromycin	30-D	UTHUKKOTTAI	NORMAL	NORMAL	NO	YES.[recently admiited and treated as in patient for CVA in hospital]	Residual hemiparesis [CVA]	MEDICAL	IMPROVED	DEFINTE	yes
102536	38	F	-	-	30-C	CHENNAI	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	yes
85962	46	F	chlorompenicol,tetracyclin,vancomycinMIC,linezolid,ciprofloxacin,rifampin,	erythromycin,clindamycin,cotrimaxazole, pencillin,gentamycin	206/CARDIO CCU	ARCOT	NORMAL	NORMAL	NO	NO	STROKE [CVA]	MEDICAL	IMPROVED	DEFINTE	0
58579	37	M	vancomycin,linezolid.chlorompenicol , rifampin,Highlevel gentamycin,ampicillin	,erythromycin	N5/CARDIOCCU	TVNMLI	NORMAL	NORMAL	NO	NO	STROKE .[CVA]	MEDICAL	IMPROVED	DEFINTE	0
62865	20	M	-	-	C-30D	KANCHIPURAM	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	0

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50194	20	F	-	-	C3-30-C	SALEM	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	POSSIBLE	yes
75127	24	F	-	-	30-C-C1	TVNMLI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	POSSIBLE	yes
78487	42	M	-	-	C-1 -30-C	CHENNAI	ABNORMAL	NORMAL	NO	NO		MEDICAL	IMPROVED	DEFINTE	yes
73426	65	M	-	-	123/M1/CARDIO CCU	CHENNAI	NORMAL	NORMAL	NO	NO	DIGITAL GANGRENE.	MEDICAL	IMPROVED	POSSIBLE	yes
46190	37	M	-	-	CCU	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	SURGICAL	DIED	DEFINTE	yes
30896	28	M	tetracyclin,ciprofloxacin,linezolid, rifampin,vancomyciMIC,chloromphenicol	erythromycin,clinndamycin ,cotrimaxazole, pencillin,gentamycin	C-4-30D	TVNMLI	NORMAL	NORMAL	NO	YES. [recently admiited and treated as in patient for CVA in hospital]	residual hemiparesis [CVA]	MEDICAL	AMA	POSSIBLE	0
11299	65	F	-	-	30-C	TVNMLI	NORMAL	NORMAL	NO	NO	CCF	SURGICAL	AMA	DEFINTE	yes
161017	37	M	.	.	30-D	TVNMLI	NORMAL	NORMAL	YES	YES .[Treated as inn patient for morethan 10 days for snake bite]	NIL	MEDICAL	IMPROVED	DEFINTE	yes
41922	40	F	.	.	30-C	VELLORE	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	DEFINTE	0
77654	42	M			30-D	TINDIVANAM	NORMAL	ABNORMAL	NO	YES. [on regular dialysis and follow up]	RENAL FAILURE[.ACUTE ON CHRONIC]	MEDICAL	IMPROVED	DEFINTE	yes
84916	22	F	.	.	211/CARDIOCCU/ NEPHRO	VILLUPURAM	NORMAL	ABNORMAL	NO	YES. [On regular dialysis]	CCF+ RENAL FAILURE [ACUTE ON CHRONIC]	MEDICAL	NOT ON FOLLOW UP	POSSIBLE	yes
74675	23	F	.	.	N5/CARDIO30-C	VILLUPURAM	NORMAL	NORMAL	NO	NO	STROKE [CVA.]	MEDICAL	AMA	DEFINITE	0
6760	25	M	.	.	CCU-C5	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	NOT ON FOLLOW UP	DEFINITE	yes
27421	44	F	.	.	30-C-C1	ARAKKONAM	NORMAL	NORMAL	NO	NO	-	MEDICAL	IMPROVED	POSSIBLE	yes
7582	40	M	ceftriaxone,pencillinMIC,vancomycin ,chloromphenicol, linezolid,erythromycin,clindamycin	tetracyclin,ofloxacin	CCU.	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	DEFINITE	0
12469	33	M	.	.	225/CARDIOLOG YCCU	VANDAVASI	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	NOT ON FOLLOW UP	DEFINITE	yes
8005	30	F	..	..	30-C-C5	KANCHIPURAM	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	0

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1587	21	M	..	..	STROKE WARD/CCU	CHENNAI	NORMAL	NORMAL	NO	NO	STROKE [CVA.]	MEDICAL	IMPROVED	POSSIBLE	yes
2277	50	M	meropenem,ceftriaxone, amikacin, gentamycin, tetracyclin, piperacillin tazobactum	ciprofloxacin,cotrimaxazole,chloromphenicol	CCU	TVNMLI	NORMAL	NORMAL	NO	YES. [Recently admited as inpatient in hospital for stroke]	Rresidual hemiparesis [CVA]	MEDICAL	IMPROVED	DEFINITE	0
13886	75	M	..	..	30-D	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	DEFINITE	0
61240	27	M	..	..	CT PO1/CARDIOLOGY	KANCHIPURAM	NORMAL	NORMAL	YES	YES[ecently treated for craniotmy]	NIL	MEDICAL	NOT ON FOLLOW UP	POSSIBLE	yes
60414	19	M	.	..	ICCU/C2/CT6	TIRUVALUR	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	DEFINTE	yes
78635	64	F	..	..	CCU	VANDAVASI	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	NOT ON FOLLOW UP	POSSIBLE	0
7308	38	F	.	..	ICCU-C3	TIRUVALUR	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	yes
124325	48	M	..	..	30-D	ARAKONAM	NORMAL	NORMAL	NO	NO		MEDICAL	NOT ON FOLLOW UP	DEFINITE	yes
86619	32	F	..	..	ICCU.	TVNMLI	NORMAL	ABNORMAL	NO	YES . [pt on regular dialysis]	CCF+RENAL FAILURE[ACUTE ON CHRONIC]	MEDICAL	NOT ON FOLLOW UP	POSSIBLE	yes
69971	20	F	..	..	30-C	KODUVANGERI	NORMAL	NORMAL	NO	NO		MEDICAL	NOT ON FOLLOW UP	DEFINITE	0
15571	35	F	gentamycin, ciprofloxacin, vancomycinMIC,rifampin,linezolid,tetracyclin	erythromycin,clindamycin,cotrimoxazole,pencillin,chloromphenicol	123-M3/CARDIO CCU	KANCHIPURAM	NORMAL	NORMAL	NO	NO		MEDICAL	NOT ON FOLLOW UP	DEFINITE	0
15519	55	M	..	..	225-M3/CARDIO	ARIYALOR	NORMAL	NORMAL	NO	YES		MEDICAL	IMPROVED	POSSIBLE	yes
17840	40	M	..	..	30C-C1	TIRUVALUR	NORMAL	NORMAL	NO	NO	CCF	SURGICAL	DIED	DEFINITE	0
32071	28	F	erythromycin.rifampin.vancomycinMIC,linezolid, gentamycin,tetracyclin.clindamycin,pencillin	ciprofloxacin,cotrimaxazole,chloropenicol	121-M6/CARDIOLOGY CCU	VILLUPURAM	NORMAL	NORMAL	NO	YES	CCF	MEDICAL	IMPROVED	DEFINITE	0
23428	24	F	..	..	30-C C 1	TVNMLI	NORMAL	NORMAL	NO	YES	NIL	MEDICAL	IMPROVED	POSSIBLE	yes

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33173	62	M	.	.	30-D	CHENNAI	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	0
32988	20	M	..	..	30-D	TIRUVALUR	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	NOT ON FOLLOW UP	DEFINITE	yes
40382	20	M	..	..	125/NEURO/CARDIO	VELLORE	NORMAL	NORMAL	NO	NO	STROKE[CVA] .	MEDICAL	IMPROVED	POSSIBLE	yes
43072	37	F	..	..	30-C/NEURO	CHENNAI	NORMAL	NORMAL	NO	NO	STROKE [CVA.]	MEDICAL	IMPROVED	DEFINITE	yes
46841	47	F	..	..	CCU/NEPHRO	PERAMBALUR	NORMAL	ABNORMAL	NO	YES.[ON HEMODIALYSIS FOR CRF]	CCF+RENAL FAILURE[ACUTE ON CHRONIC]	MEDICAL	NOT ON FOLLOW UP	POSSIBLE	yes
44275	28	M	..	..	30-DC3	COIMBATORE	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	NOT ON FOLLOW UP	DEFINITE	yes
47026	28	F	..	..	30-C	CHENNAI	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	yes
39920	45	M	..	..	CCU.	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	AMA	DEFINITE	0
23009	46	M	..	..	30-D	ARIYALUR	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	DEFINITE	yes
61214	54	M	..	..	CTS5/CARDIO	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	SURGICAL	AMA	DEFINITE	yes
73672	50	M	..	..	CCU	CHENNAI	NORMAL	NORMAL	NO	NO		MEDICAL	IMPROVED	POSSIBLE	0
11852	71	F	..	..	30-C-C2	CHENNAI	NORMAL	NORMAL	NO	NO	CCF	MEDICAL	IMPROVED	POSSIBLE	yes
63246	21	F	..	..	30-C	NAGAPATINAM	NORMAL	NORMAL	NO	NO	NIL	MEDICAL	IMPROVED	POSSIBLE	0